DEPARTMENT OF PEDIATRICS

2005

SPECTRUM OF RESPIRATORY DISTRESS DISORDERS IN NEONATES

SUMMARY

THESIS

FOR

DOCTOR OF MEDICINE
(PEDIATRICS)

BUNDELKHAND UNIVERSITY
JHANSI (U.P.)

VIVEK KUMAR CHETAL

Summary and Conclusions

The present study was conducted on 50 neonates, admitted in NICU of the Department of Pediatrics, M.L.B. Medical College, Jhansi from November 2003 to October 2004, with respiratory distress. The present study was undertaken with the following aims:

1. To find the causes of respiratory distress in neonates brought to our Neonatal Intensive Care unit with symptoms suggestive of respiratory disorder.
2. To evaluate clinical signs like cough, difficulty in feeding, cyanosis, respiratory rate, chest retractions, flaring of alae nasi and adventitious sounds for diagnosis of neonatal pneumonia.
3. Determine bacterial etiology of neonatal pneumonia.
4. To study the sensitivity pattern of the prevalent bacteria in neonatal intensive care unit.

The present study comprised of neonates presenting with respiratory distress delivered in the Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi and elsewhere, but admitted in our Neonatal Intensive Care Unit (NICU). The study was conducted on the spectrum of respiratory distress, signs and symptoms,

clinical history and investigations suggestive of four disorders, i.e. Pneumonia, Transient tachypnoea of the newborn, Hyaline membrane disease (HMD) and Meconium aspiration syndrome (MAS).

The blood samples were taken from the peripheral vein for investigations, and were subjected to sepsis screen (TLC, DLC, Micro-ESR, CRP, Band cells and toxic granules), blood culture. The samples were send to the emergency pathology and Department of Microbiology, M.L.B. Medical College, Jhansi for investigations. The neonates were send for radiological investigations also.

- In our study, pneumonia was the leading cause of respiratory distress with an incidence of 46%, followed by Hyaline Membrane Disease (HMD) 42%, Meconium Aspiration Syndrome (MAS) 8%, and Transient Tachypnoea of Newborn (TTNB) 4% respectively. Respiratory distress formed 30% of all the admissions to our NICU.
- The male : female ratio of neonates developing respiratory distress was 2.3:1.
- The mean birth weight for neonates developing pneumonia was 2.2 Kg, 1.4 Kg for Hyaline Membrane Disease (HMD), 3.02 Kg for Meconium Aspiration Syndrome (MAS) and 2.6 Kgs for Transient Tachypnoea of Newborn (TTNB)

- 14 (60%) of our cases developing pneumonia were fullterm, while nine (40%) were preterms in this study.
- In our study all the 21 neonates with Hyaline Membrane Disease (HMD) had a gestational age < 34 weeks. All the 21 neonates were low birth weight. 18 of them were less than 2000 gms and remaining 3 of them were of 2 Kg. Both weight and gestational age had the highest sensitivity (89.6%) (93.1%) and negative predictive value (89.6%) (100%) respectively for diagnosing HMD.
- Cough, adventitious sounds & cyanosis had high specificity in diagnosing neonatal pneumonia, while difficulty in feeding, RR > 60/minute, flaring of alae nasi and chest retractions had high sensitivity for diagnosing pneumonia.
- The mortality in non-tachypnoeic as compared to tachypnoeic cases was significant. In our study, of 23 cases of pneumonia, we found only two cases with RR < 60 (8.7%), but the mortality was 100% and both of them had gestational age < 34 weeks and weight < 2 Kg.
- In our study, 11 mothers had a history of Prolonged Rupture Of Membranes (PRM) (10), maternal fever (2), leaking per vaginum (6). These factors had high specificity and positive predictive value in neonates developing pneumonia.

- None of the factors like maternal fever, prolonged rupture membranes, leaking per vaginum or foul smelling liquor was found to have any association at all with transient tachypnoea of newborn (TTNB).
- Except for a history of fetal distress, none of the factors like Prolonged Rupture of Membranes (PRM), maternal fever, leaking per vaginum (LPV) had any association at all with meconium aspiration syndrome (MAS). Fetal distress had a high specificity and negative predictive value for MAS.
- Mothers of neonates with Hyaline Membrane Disease (HMD) had association with Prolonged Rupture Of Membranes (PRM) and L P/V. In our study, 5 mothers of neonates with HMD had PRM and 5 had leaking per vaginum (L P/V). Probable explanation could be that these factors were indirectly also responsible for preterm labour and birth.
- Prolonged labour has a high specificity (88.8%) for neonates having pneumonia.
- Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with Transient Tachypnoea of Newborn (TTNB).

- Prolonged labour and a history of poor cry or resuscitation in newborn have a high specificity for Meconium Aspiration Syndrome (MAS). History of poor cry in natal history had a 100% positive predictive value (PPV) for neonates developing respiratory distress due to MAS.
- Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with Hyaline Membrane Disease (HMD) in our study.
- 28% of all neonates with respiratory distress were delivered at home, while 43.5% of all cases with pneumonia were delivered outside by Dais or P/V in hospitals by untrained staff having meager facilities.
- We also found that 3 out of 4 neonates (75%) having MAS were delivered by emergency LSCS, the indication was prolonged labour in all three of them. Both the neonates with TTNB in our study were delivered in the hospital by emergency LSCS. 18 cases of HMD were delivered in hospital, because most of them had to be delivered by emergency LSCS.
- History of difficulty in feeding in the post natal period with fever had a high specificity for diagnosing pneumonia. Fever, absence of post maturity also had a high specificity, but 0% sensitivity, in the case of post maturity.

- In our study meconium staining of cord, liquor and nails had a 100% sensitivity, specificity and predictive value for MAS. Post maturity (n=2 out of 4) also had a 100% specificity and positive predictive value in cases diagnosed as MAS.
- Apart from a difficulty in feeding (50%), none of the other post natal factor could be associated with TTNB.
- 100% cases later diagnosed as TTNB presented with respiratory distress within 4 hours of birth.
- We found the values for sensitivity (60%), specificity (92.6%), PPV (87.5%) and NPV (73.5%) for CRP. In comparison to other indicators of infection, CRP is the single best indicator after blood culture in diagnosing early onset sepsis (EOS).
- Specificity for Micro-ESR was 100% and sensitivity 26%.
- With band cells and toxic granules, our specificity was > 90% but sensitivity was very low 13%.
- In the present study, the percentage of definitive pneumonia (based on isolation of bacteria) and probable pneumonia (blood culture negative) were 39.1 and 34.8% respectively.
- In 8.7% cases of pneumonia only sepsis screen was positive.
- Amongst 17 x-ray chest positive cases in pneumonia, 11 cases showed alevolar infiltrates (47.8%), 4 cases showed diffuse haziness

(17.3%), 2 cases showed lobar consolidation (8.6%), while 6 cases had chest x-ray clear (26.1%).

- ❖ Chest x-ray and clinical signs alone would have missed the diagnosis of pneumonia in 26% cases and these had to be corroborated with sepsis screen and blood culture.
- ❖ X-ray chest was positive in 50% cases of TTNB. Chest x-ray showed changes pertaining to Meconium aspiration syndrome (MAS) in 50% cases. In HMD, only 33.3% cases turned out to be chest x-ray positive. Rest of the blood investigations were negative in all these three disorders i.e. Hyaline Membrane Disease (HMD), Transient Tachypnoea of newborn (TTNB) and Meconium aspiration syndrome (MAS).
- ❖ The bacterial isolates in our study suggest an increasing trend of Klebsiella (61.5%).
- ❖ In the present study Staphylococcus aureus was found only in 2 cases (15.4%), while E.coli was responsible for pneumonia in 3 cases (23.1%),
- ❖ Respiratory distress was responsible for 28.7% of all deaths The mortality figures were 52% for HMD in our study and 75% for Meconium Aspiration Syndrome (MAS).

- There were 39% low birth weights (< 2.5 Kg) in pneumonia. They comprised 57.1% mortality amongst total fatality due to pneumonia. Since, there were 2 neonates with birth weight less than 2 Kg having pneumonia and both of them expired the mortality rate was 100%. 11 (52.4%) neonates out of 21 with HMD expired in our study, all of them were of low birth weight.
- The best coverage in our study, has been shown by ciprofloxacin (84.62% cases) followed by ofloxacin and chloramphenicol 76.92% and 61.5% respectively. Amikacin was effective in only 23.08% cases.
- Further long-term studies have to be done before our studies on the efficacy and long-term complications of Ciprofloxacin in treating neonates with pneumonia could be finally established.

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2005

VIVEK KUMAR CHETAL

CERTIFICATE

This is to certify that the work entitled ***" Spectrum of Respiratory Distress disorders in neonates"*** has been carried out by ***Dr. Vivek Kumar Chetal*** in the Department of Pediatrics, M.L.B. Medical College, Jhansi. He has put in the necessary stay in the Department as per University regulations, and has fulfilled the conditions required for the submission of thesis according to University regulations.

Dated: 30 / 10 / 2004

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CERTIFICATE

This is to certify that the work entitled ***" Spectrum of Respiratory Distress disorders in neonates "*** which is being submitted as a thesis for M.D. (Pediatrics) Examination 2005 of Bundelkhand University, Jhansi, has been carried out by ***Dr. Vivek Kumar Chetal*** under my direct supervision and guidance.

The techniques embodied in the thesis were undertaken by the candidate himself and the observations recorded have been checked and verified by me from time to time.

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The techniques embodied in the thesis were undertaken by the candidate himself and the observations recorded have been checked and verified by me from time to time.

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Dated : 30|10|2004

Dr. Vivek Kumar Chetal.

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Introduction

Introduction

Respiratory distress is one of the commonest disorders encountered within the first 48 - 72 hours of life. It occurs in 0.96 to12% of live births and is responsible for about 20% of neonatal mortality. Respiratory pathology is the commonest (32-54%) autopsy finding among early neonatal deaths. The spectrum of respiratory distress in neonates includes pneumonia, transient tachypnea of the newborn, hyaline membrane disease, meconium aspiration syndrome and other miscellaneous causes. The male: female ratio was found to be 2:1.The higher incidence in male is probably due to their bigger size and relative immaturity as compared to female infants of same weight group. In developing countries there is a paucity of studies on causes of respiratory distress in neonates and all respiratory distress in neonates are treated as pneumonia at the first referral unit.

The importance of respiratory distress in the neonates can be realized from the fact that the neonates with respiratory distress are 2-4 times more likely to die that those without respiratory distress. The knowledge of the causes of respiratory distress is important to plan facilities.

To prevent injury by microorganisms and foreign substances, a variety of defense mechanisms have evolved, both systemic and within the respiratory tract.

In the study by NB Mathur (2003), many of the defenses are compromised in the fetus and newborn infant. Newborn infants typically have sterile respiratory mucosa at birth. Access to distal respiratory structures and bypass of the ciliary escalator occurs in infants who require endotracheal intubation. In these infants, increased physical disruption of epithelial and mucous barriers also occurs. Exposure to high oxygen concentrations and airway pressures interferes with ciliary function and mucosal integrity. Secretory antibodies and mucosal lymphoid tissue are absent or minimally functional for the first month of life. Circulating complement components are present at approximately 50% of the concentration found in older children, although components of the alternative pathway are present in sufficient quantities to serve as effective opsonins. The neonatal granulocytes frequently decrease in response to early infection, while the phagocytes that are present often move much more sluggishly to the inflammatory focus. Interalveolar communications (pores of Kohn) are few in number in the neonate and become prominent only after the age of 7 years. The absence of

this 'collateral ventilation' probably increases the risk of pulmonary atelectasis in the neonate.

The diagnosis of clinical conditions producing respiratory distress is usually based mainly on careful scrutiny of the history, clinical and radiological findings.

According to Avery ME, Fletcher BD (1974), the infant with HMD is almost always premature and is cyanotic in room air. There is rapid or labored breathing beginning at or immediately after birth. The severity of respiratory distress can be represented by the Silverman score.

Infants usually have a characteristic grunt during expiration, caused by closure of the glottis, the effect of which is to maintain lung volume and gas exchange during exhalation. Frequently the unventilated infant requires 40% to 50% oxygen after birth for relief of central cyanosis but then develops an increasing oxygen requirement over 24 to 48 hours; this may reach as high as 100%.

Clements and Tooley (1977), described diffuse fine granular densities that develop during the first 6 hours of life are seen on the chest radiograph, these densities are influenced by size of the infant, severity of disease, and degree of ventilatory support. The appearance may be more marked at the lung bases than at the apices. The lung volume is decreased.

According to Avery ME, Fletcher BD (1974), HMD was a problem of insufficient lung maturity, the best way to prevent it is to prevent premature birth. 1). Prediction of the risk for HMD by antenatal testing of amniotic fluid samples, and 2). Antenatal treatment of women in preterm labor with glucocorticoid hormones to accelerate fetal lung maturation.

William H Tooley, found that the second-born twin is more likely to be affected, and a family history of HMD increases the risk for any premature infant.

Another more rapid test for lung maturity is the foam stability or shake test, which was described by Clements and associates (1975). This test is based on the ability of pulmonary surfactant to form highly stable surface films that can support the structure of a foam for relatively long periods.

Meconium is biochemically composed of a mucopolysaccharide of high blood group specificity, a small amount of lipid, and a small amount of protein that decreases throughout gestation. Its blackish green color is the result of bile pigments.

According to Nathan et al (1994), it is possible that the passage of meconium in utero is the result of transient parasympathetic stimulation from cord compression in a neurologically mature fetus.

MSAF in connection with fetal heart rate abnormalities is a marker for fetal distress and is associated with an increased perinatal morbidity.

As per Yeoman S et al (1989), if meconium is not removed from the trachea after delivery, with the onset of respiration it migrates from the central airways to the periphery of the lung. Initially, particles of meconium produce mechanical obstruction of the small airways that results in hyperinflation with patchy atelectasis. Later, small airway obstruction is the result of chemical pneumonitis and interstitial edema.

Infants with MAP are often postmature and have visible meconium staining of the nails, the skin and the umbilical cord. Many infants with MAP have been asphyxiated, and much of the early distress may relate more to asphyxia and retained fetal lung fluid complicated by elevated pulmonary vascular resistance than to the presence of meconium in the airway. Infants with MAP have clinical evidence of lung overinflation, with a barrel chest. Auscultation of the chest reveals diffuse rales and ronchi. The chest radiograph shows patchy areas of atelectasis and areas of overinflation.

Hyperaeration is evident by hyper translucence, horizontal ribs and depressed domes of diaphragm (with more than 7 intercostal spaces being visible). Findings are characteristically non-uniform and asymmetric.

Avery and associates (1966), found that persistent postnatal pulmonary edema is more common in boys. The disorder typically begins soon after birth with a rapid respiratory rate, ranging from 60 to 160 per minute, and sometimes with sternal and subcostal retractions of the chest wall, grunting, during expiration, and occasionally, mild cyanosis that disappears with the delivery of supplemental oxygen.

The radiographic picture of TTNB is characterized by prominent hilum and symmetrical streaky opacities emanating from the hila because of excess interstitial fluid. The pleural fluid tracks into the inter-lobar fissure which appears prominent. At times, there may be a small pleural effusion, minimal cardiac enlargement and mild hyperaeration.

Lower incidence of Respiratory Distress Syndrome in India and also in postmortem finding of Indian authors as compared to that of Western countries is possibly due to failure of many premature infants to survive for a certain minimum period to have developed pulmonary hyaline membrane and relative maturity of pulmonary alveolar epithelial cells in response to more corticosteroid secretion by our mothers in response to stress and higher rate of infection.

Naeye and Peter (1978), "In assessing the risk of neonatal infection to premature in premature infants, the important thing to

consider is not the length of membrane rupture but whether or not preterm labor occurred and whether or not amnionitis was present".

In transplacental pneumonia, bacteria cross the placenta and invade the fetal lungs by the hematogenous route, as in congenital syphilis and in some cases of listeriosis with maternal septicemia. In transnatal pneumonia, there is no evidence of either preceding amnionitis or maternal infection, although the infant is believed to aspirate vaginal bacteria during the birth process. The onset of clinical signs of pneumonia is delayed for a few hours or days or even longer. A true inflammatory process in the lung is always present.

S.P.Khatua et al (1979) stated that, pneumonia is diagnosed from the history of early rupture of membranes with prolonged labour, recent febrile illness of the mother or operation in a dirty place, respiratory distress, fever in a full term infant.

Thomas Hansen and Anthony Corbet (1988), observed that the usual clinical picture is that of respiratory distress with onset at or soon after birth. Sometimes, however, the onset of respiratory distress is delayed, preceded by increasing tachypnea during the 1st day of life. Infants with infection often have poor peripheral perfusion and tachycardia.

Other signs are abdominal distention, temperature instability, unexplained metabolic acidosis, or excessive jaundice. Some infants progress to a state of septic shock.

The positive gastric aspirate is not diagnostic of pneumonia: it indicates only increased risk.

The gastric aspirate can also be evaluated with the foam stability (shake) test. If the test is positive, pneumonia is more likely (and RDS is very unlikely). A negative test may not distinguish between RDS and pneumonia.

Sherman et al (1980), stressed that, the blood culture should be done in all cases of suspected pneumonia as well as cerebrospinal fluid analysis because meningitis may also be present.

Sometimes the radiograph initially is normal, but later films show abnormalities developing over the first few days; this course is suggestive of a transnatal pneumonia.

NB Mathur et al (2003), found that the organisms responsible for pneumonia mirror those responsible for early-onset neonatal sepsis. Group B Streptococcus has been the most common bacterial isolate in the west. However, Group B Streptococcus is not commonly seen in India. Commonly implicated bacterial organisms in India include Klebsiella pneumoniae, Escherichia coli and Staphylococcus aureus. Transplacental pneumonia usually occurs in association with

congenital syphilis, cytomegalovirus, herpes virus, rubella, toxoplasma, listeria monocytogenes and mycoplasma infections. These infants show involvement of many organ systems and manifestations of pneumonitis may be obscured. Chlamydia is presumably transmitted at birth during passage through an infected birth canal, although most infants are asymptomatic during the first 24 hours and develop pneumonia only after the first 2 weeks of life.

Respiratory pathogens, such as respiratory syncytial virus, influenza, adenovirus, and others, may be transmitted by contact with infected family members or caregivers shortly after birth, but infection by these organisms rarely is manifested during the first 24 hours. Frequency of neonatal pneumonia due to chlamydia and viruses has not been evaluated in India.

Hallahakoon and Halliday (1995), observed that with transplacentally acquired infection there are diffuse, interstitial opacities giving a ground glass, reticular pattern which may be indistinguishable from RDS or there may be extensive consolidation. With ascending infection there may be alveolar involvement which produces bilateral coarse opacities which are much less uniform.

Pneumonia acquired following aspiration is usually less evenly distributed on chest radiograph and may show as segmental or lobar collapse.

Early contrast radiography studies show that 10-15% of newborn babies aspirate fluid into their lungs during the first few days after birth.

Aspiration can occur before birth and amniotic debris including squamous cells have been found in the lungs of stillborn babies. Aspiration of small amounts of fetal and maternal blood do not appear to cause major problems and are rapidly removed from the lungs. If purulent secretions are aspirated during birth there is an increased risk of subsequent bacterial pneumonia. Aspiration of milk may occur in the very preterm infant, those with swallowing disorders (Goodwin et al, 1985).

A number of factors may interfere with the ability to cultivate a likely pathogen from the sites noted, including the following: (i) pretreatment with antibiotics that limit in vitro but not in vivo growth, (ii) contaminants that overgrow the pathogen, (iii) pathogens that do not replicate in currently available culture systems, (iv) sampling of an inappropriate site, and (v) patients in whom the process is inflammatory but not infectious, such as with meconium aspiration.

Since the risk is increased, aspiration lung technique is usually reserved for circumstances in which empiric therapy fails after several days, less invasive cultures and detection tests are unrewarding, or the infant continues to deteriorate.

Mathur et al (2002) found that the presenting complaints in neonates with pneumonia include rapid breathing (83.4%), poor feeding (81%) and difficult breathing (79.1%). In primary neonatal care rapid breathing, poor feeding and difficult breathing are useful symptoms suggestive of respiratory distress. Presence of cough is significantly different in neonates with pneumonia, as compared to neonates with respiratory distress due to other causes. Cough, adventitious sounds and flaring of alae nasi had high specificity, while chest retractions, difficulty in feeding and RR > 60 have high sensitivity for diagnosis of pneumonia in neonates.

Earlier studies on neonatal pneumonia have included neonates with only radiological findings and have not considered blood culture positivity in diagnosis of neonatal pneumonia .Webber et al, however, had classified neonatal pneumonia as "definitive pneumonia" if respiratory pathogen was isolated from the blood and "probable pneumonia" if blood culture failed to show any pathogen, in presence of a positive chest X-ray. No earlier study has stated detailed diagnostic criteria for pneumonia in neonates utilizing blood culture or sepsis screen positivity. The National Neonatology Forum have included them in the diagnostic criteria but have not done any study evaluating utility of these criteria separately for diagnosis of pneumonia in neonates. Furthermore the diagnosis of pneumonia

based on a respiratory rate of more than 60 prescribed by the W.H.O. would also miss a significant number of cases.

A study done by Mathai et al (2004), regarding association between intrapartum risk factors for infection with CRP levels showed that several such risk factors can cause elevated CRP levels in the absence of infection. Since CRP does not cross placenta, the elevated levels are due to production of CRP in the neonate. Chorioamnionitis can result in elevation of IL-6 levels even in uninfected neonates. Stimuli other than infection, like hypoxia, trauma and metabolic changes can also induce production of proinflammatory mediators. This cytokine stimulates CRP production.

A prenatal risk score depending upon the foul smelling liquor, unclean vaginal examination done before delivery, duration of labour exceeding 24 hours, one minute apgar score of 0-6, duration of rupture of membrane before delivery exceeding 24 hrs., birth weight 2 kg or less and / or gestation less than 37 weeks can decide the amount of risk a neonate is exposed. Antibiotics can be safely withheld in the low risk group while antibiotics should be started in the high risk group infants. The moderate risk group must be investigated for the presence of infection and depending upon the circumstantial evidence may be given antibiotics.

Improved antenatal supervision, timely treatment of maternal diseases, improved obstetrical and neonatal management will go a long way in reducing the incidence of respiratory distress in newborn.

Aims

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Objectives

Aims and Objectives

1. To find the causes of respiratory distress in neonates brought to our Neonatal Intensive Care unit with symptoms suggestive of respiratory disorder.
2. To evaluate clinical signs like cough, difficulty in feeding, cyanosis, respiratory rate, chest retractions, flaring of alae nasi and adventitious sounds for diagnosis of neonatal pneumonia.
3. Determine bacterial etiology of neonatal pneumonia.
4. To study the sensitivity pattern of the prevalent bacteria in neonatal intensive care unit.

Review Of Literature

Review of Literature

Respiratory distress presents a major threat to the survival of the-newborn and contributes inestimably to morbidity in this age group. S.P. Khatua et al (1979) reported that though the overall incidence of respiratory distress was 6.9 /1000 live birth, it was 30.45 and 5.37 in premature and mature infants respectively .indicating that the incidence in premature was 6 times more common than in term infants. Driscoll & Smith (1962) noted respiratory distress accounting for about half of the neonatal death. Higher incidence of respiratory distress ranging from 2.92% - 3.9% was also noted by other workers.

In an autopsy study of 422 cases, Driscoll & Smith observed lung disorder in 63% cases of which hyaline membrane disease was in 60% cases, pneumonia in 14% cases and massive aspiration in 3% cases. Prenatal mortality study in India by various authors revealed respiratory disorders as the cause of death in 13% -54% cases. In order of frequency, the important causes were pneumonia, pulmonary hemorrhage aspiration and H.M.D.

Prod'hom et al (1974) in their study of 1402 cases of respiratory distress with a birth weight of 2 kg. or less found H.M.D. in 42.2%, transient tachypnea in 30%, aspiration syndrome in 16 % and symptomatic cases like pneumonia, malformation in 10.9% cases.

Hyaline Membrane Disease

Schaffer (1971) found respiratory distress syndrome as the leading cause of respiratory distress limited almost entirely to premature.

Cunningham and Smith (1973) in their study of 137 cases requiring transport to special ward observed 78 cases of respiratory disorder, of which 73% were due to R.D.S. and 23% due to massive aspiration.

H.M.D is more common in male than in female infants (Miller and Futrakul, 1968); it is more common in white than in nonwhite infants (Richardson and Torday, 1994).

At any given gestational age, the incidence is higher for cesarean section without labor than for vaginal delivery (Fedrick and Butler, 1972). There is a significantly increased risk if elective cesarean section is performed before completion of 39 weeks gestation (Morrison et al, 1995).

Most infants of diabetic mothers are large for gestational age, and similarly over nourished infants in the absence of maternal diabetes are also at increased risk (Naeye et al, 1974). When corrected for the important effect of gestational age, the occurrence of HMD is significantly increased in gestational diabetes and in insulin-dependent mothers without vascular disease (Robert et al, 1976).

Early reports in comparatively large infants suggested that the risk is decreased in infants who are small for gestational age (Gluck and Kulovich, 1973); however, in much less mature infants seen, comparisons of appropriate-for-gestational-age and small-for-gestational-age infants, both weight matched and gestation matched, suggest that immature small-for-gestational-age infants do not have this advantage (Pena et al, 1988). In fact, there is some evidence that the risk of RDS at constant gestational age may be increased in small-for-gestational-age infants and that the mortality may be higher (Thompson et al, 1992; Tyson et al, 1995).

Cause of hypoxia in infants is the presence of an open, poorly ventilated lung compartment with extremely low V/Q, representing a significant portion of the lung and producing variable hypoxic vasoconstriction and alterations in right-to-left shunt as the inspired oxygen changes (Corbet et al, 1974).

In preterm infants without RDS, the ductus arteriosus tends to close within 4 days of birth (Reller et al, 1988), whereas in RDS the ductus tends to remain open (Reller et at, 1993) and may become a significant problem by 3 to 4 days of age (Corbet, 1996).

Infants do not grunt with every breath, and those with severe disease grunt most frequently. By maintaining a positive intrapulmonary pressure during most of the respiratory cycle, grunting

probably helps to prevent atelectasis. When not grunting, infants with HMD have small tidal volumes and a rapid respiratory rate.

Jobe et al, showed that the combination of antenatal corticosteroids and surfactant replacement therapy reduced morbidity and mortality rates to very low levels in a group of preterm infants.

Maternal conditions that compromise fetal growth and may produce, decreased risk include pregnancy induced hypertension, chronic hypertension, sub-acute placental abruption, narcotic addiction, and maternal smoking, Tubman and colleagues (1991) found an increased risk for RDS in infants of hypertensive mothers.

Edberg and coworkers (1991) found decreased compliance, increased resistance, decreased lung volume and reduced gas mixing efficiency in very-low-birth-weight infants with RDS.

In infants who die, deMello and associates (1987) has demonstrated the complete absence of tubular myelin and a modest deficiency of lamellar bodies in Type – 2 cells in comparison with controls.

Meconium aspiration syndrome

Meconium staining of the amniotic fluid is found in about 9% of deliveries at term, and at birth 56% of these babies have meconium in their tracheas (Gregory et al, 1974).

S.P.Khatua et al (1979), found that the higher incidence of aspiration syndrome in this study was due to poor antenatal care, higher number of referred cases with prolonged labour, failed medical induction, abnormal labour and accidental hemorrhages, all of which predispose to perinatal asphyxia with aspiration.

Airway resistance is increased in newborn infants and experimental animals with MAP (Tran et al, 1980; Yeh et al, 1982). In addition, dynamic lung compliance is reduced while static lung compliance is unchanged, suggesting that airway obstruction is patchy and located in peripheral airways.

Early data suggested that meconium did not impair surfactant function (Tran et al, 1980), more recent data suggest that meconium does inactivate surfactant (Davey et al, 1993; Moses et al, 1991; Sun et al, 1993a).

Meconium is aspirated into the tracheobronchial tree when the fetus begins to gasp deeply in response to hypoxia and acidosis. Data showing that cord arterial pH is lower in meconium-stained infants with meconium in their tracheas at delivery supports this hypothesis (Yeomans et al, 1989).

According to Cleary GM et al (1990), neonates with meconium aspiration syndrome and umbilical pH ≥7.20 at delivery developed seizures as often as those with pH <7.20 (20.1% vs. 21.1%; P = 1.0).

Normal acid-base status at delivery is present in many cases of severe meconium aspiration syndrome, which suggests that either a preexisting injury or a nonhypoxic mechanism is often involved.

Studies on meconium aspiration syndrome have led to the speculation that asphyxial episodes too brief to decrease pH or Apgar scores may cause the passage of meconium in utero. These conclusions were supported by a study showing that there was no correlation between the consistency of meconium and markers of fetal asphyxia (Trimmer and Gilstrap, 1991).

There is usually slow radiological clearing over 10 days but in some babies the meconium disappears within 2 – 3 days possibly by ciliary action, phagocytosis or enzymatic lysis (Halahakoon and Halliday, 1995).

Studies have suggested that when thick meconium staining has occurred the obstetrician should suck out the mouth as the head crowns, using either a suction catheter or a bulb suction. Gregory et al (1974) found that 56% of meconium stained infants had meconium in the trachea and in 10% there was meconium below the cords despite it being absent from the mouth or pharynx. "Compared with expectant management intubation and suctioning of the apparently vigorous meconium stained infant does not result in a decreased incidence of

MAS or other respiratory disorders. Complications of intubation are infrequent and short lived."

A large randomized study, showed no benefit of routine endotracheal intubation in these circumstances and indeed the babies whose airways were aspirated had more respiratory problems than the control infants (Linder et al, 1988).

In a study by Zagariya A et al (2004), meconium instillation caused significant expression of inflammatory cytokines TNF, IL-6, and IL-8 ($p<0.05$) with a peak of 8 hours after meconium instillation. Levels of IL-10 were insignificant ($p > 0.05$). Also significant increase in necrotic cells and neutrophils ($p < 0.05$), compared to the control, saline instilled rabbit lungs.

Because meconium must ultimately be removed by phagocytes, respiratory distress and requirements for supplemental oxygen may persist for days or even weeks after birth. Infants who present with a shorter course and with rapid resolution of symptoms are more likely to have had retained fetal lung fluid than MAP.

Transient Tachypnea of Newborn

In 1966, Avery and associates described the clinical and radiographic features of eight babies with transient neonatal tachypnea, a condition that the authors attributed to delayed

absorption of fetal lung liquid. Cells from rabbits that were born prematurely or without prior labor did not exhibit increased Na^+, K^+ - ATPase activity, which is an observation that may help to explain the lung fluid retention often associated with premature birth. Around the time of birth, the long epithelium switches from a predominantly Cl – secreting membrane to a predominantly Na^+ absorbing membrane, with a resultant reversal of the direction of liquid flow.

Neonatal Pneumonia

While Benirschke (1960), had shown that apparent or inapparent maternal bacteremia could produce infection. Blane (1961), demonstrated that antenatal infection in these situations resulted from the hematogenous dissemination, the microorganisms being carried on the maternal circulation to the intervillous spaces of the placenta and thence into the blood stream. Their observations has been corroborated by Gotoff and Behrman (1970), as well, who further observed that while this was the usual mode of intrauterine viral infections, bacterial infection of the fetus generally did not follow this route. Listeria monocytogenes and vibrio fetus, however, were the possible exceptions (Gotoff and Behrman, 1970).

Blanc (1959), Benirschke (1959), Pryles (1963), Ramos and Stern (1969), Gotoff and Behrman (1970) and Habel et al (1972),

commented upon the association between the early rupture of membrane, prolonged labour and excessive manipulation infection of amniotic fluid resulting in fetal infection. However, Blanc (1959), gave a comprehensive account of the progress of events leading to whet he termed "Amniotic Infection Syndrome". The process according to him started at the internal OS with or without intact membranes and comprised of polymorphonuclear infiltration of amnion and chorion. The infection then spread to placenta and occasionally involved the umbilical vessels as well. Demonstration of polymorphonuclear infiltration of placental tissue, chorion and gastric aspirate (Blanc, 1961) were all pointers to the fact that the baby was coming from an infected environment.

Wilson (1964), Overbach (1970) therefore advocated routine examination of the placental end of the umbilical cord, as a screening test for evidence of ascending infection.

The strong association of amnionitis with premature birth may be due to a developmental deficiency of bacteriostatic factors in amniotic fluid (Schlievert et al, 1975).

Most cases of amnionitis, however, are not associated with pneumonia in the newborn. In some infants, aspiration of infected amniotic fluid occurs, but the lung parenchyma is not invaded by pathogens. As a result, neutrophils of maternal origin are confined to

the air spaces, fetal neutrophils do not infiltrate the septal walls, and fibrinous exudate does not occur. Blood culture in these infants is negative, and the clinical picture is that of fetal asphyxia, with or without postasphyxial pulmonary edema.

With an increasing latent interval between rupture of membranes and labor, the incidence of clinical amnionitis also increases (Burchell, 1964) as well as the frequency of bacteremia is cord blood samples collected at birth (Tyler and Albers, 1966).

S.P.Khatua et al (1979) reported that aspiration syndrome was the commonest cause of respiratory distress and was found in 57.1% cases followed by pneumonia in 9.35% and R.D.S. in 8.8% cases. Incidence of pneumonia was quite high (9.35%) in this series. Two infants had intra uterine pneumonia and both of them had the history of prolonged membranes rupture. The rest 15 cases had prenatally acquired pneumonia and most of them had history of either prolonged labour or difficult delivery.

A prolonged interval between rupture of membranes and the onset of labor is a significant independent factor favoring an increased incidence of amnionitis only for gestation of 37 weeks or more (Johnson et al, 1981).

In fact, infection may be one of the causes of premature labor because amnionitis often occurs in the presence of intact membranes (Naeye and Peters, 1978).

Infants of mothers with active urinary tract infection in the 2 weeks before birth are at increased risk for amnionitis (Naeye, 1979a).

The absence of labor and delivery by cesarean section are associated with a greatly reduced risk of amnionitis and of congenital pneumonia (Avery, 1984). Data also suggest that obstetric digital examinations after rupture of membranes significantly increase the chance of amniotic infection (Schutte et al, 1983). Amnionitis is more common in undernourished populations, perhaps because bacteriostatic factors may be lacking in the amniotic fluid (Naeye and Blanc, l970).

The pneumonia occurring in infants infected with L. monocytogenes may be transplacental, postamnionitis, or transnatal in type. In transplacental pneumonia, granulomatous disease of the placenta is present. The amniotic fluid in Listeria amnionitis has a greenish or chocolate-brown appearance. The chest radiograph shows a diffuse reticulonodular pattern of pneumonia if the onset is intrauterine. In transnatal pneumonia, the chest radiograph shows a bronchopneumonia pattern (Gordon et al, 1970).

The onset of pneumonia caused by Chlamydia trachomatis is usually delayed until 1 to 3 months of age, it is considered to be a transnatal pneumonia, the pathogen being acquired from the mother's vagina at delivery (Gilbert, 1986). About 2% to 10% of pregnant women have vaginal colonization with Chlamydia; in a San Francisco study, the rate was 4.7% (Schachter et al, 1986). In infants of colonized mothers, about 35% develop conjunctivitis, and 20% may develop pneumonia (Schachter et al, 1979).

In a study by **S Webber** et al (1990), all babies admitted to the neonatal unit during a period of 41 months were prospectively studied to find out the incidence, aetiology, and outcome of neonatal pneumonia, and the value of routine cultures of endotracheal tubes. Pneumonia of early onset (before age 48 hours) occurred in 35 babies (incidence 1.79/1000 live births). In 20 (57%) it was caused by group B streptococci. Blood cultures showed the presence of organisms in 16 of the 35 (46%). Endotracheal tube colonisation had occurred in 94% of these, most commonly by Gram negative organisms and Staphylococcus epidermidis. In only one of seven cases with simultaneous bacteraemia was the same organism grown from cultures of the blood. Ten babies with pneumonia of early onset (29%) died; all were preterm infants.

There have been isolated reports of congenital pneumonia caused by Ureaplasma urealyticum (Brus et al, 1991; Panero et al, 1995; Quinn et al 1985; Ursi et al. 1995; Waites et al, 1989) and Mycoplasma hominis (Ursi et al, 1995). Mycoplasma and ureaplasma are commonly associated with amnionitis in the mother; the pneumonia has an early onset, but the specific diagnosis may be made comparatively late in the clinical course. The organisms are cultured only with special media after a period of 3 to 5 days.

Gotoff and Behrman (1970), Xanthau (1972) and Steigbigel et al (1974) reported that WBC count has a wide range of normal values in the newborn period. Leucopenia (< 4000 WBC / cmm) or leukocytosis (> 25000 WBC/cmm) support a diagnosis of infection, but absence of a marked leukopenia, or leukocytosis does not rule out the possibility of septicemia. Boyles et al (1978), have suggested that leukopenia of < 10,000 cells/cmm is associated with infection in first day of life.

Marsh et al (1967), Xanthau (1972), Akanzua et al (1974) observed that change in the ratio of non-segmented to segmented neutrophils in the blood were sensitive index of the severity of the infection than the increase in the granulocyte series. Marce et al (1979) showed that the values of band cells / neutrophil ratio is 0.14 when associated with group B. β haemolyticus streptococcus infection. They documented values up to 0.17 upto first day of life.

Philip and Hemit (1980), Namdeo et al (1985), Paul et al (1986) and Chandra et al (1988) observed similar findings in their study.

Evans et al (1970), reported that M-ESR is a simple inexpensive test requiring only capillary blood and hence ideally suited for newborn infants. ESR is a non-specific indicator of infection. The sedimentation rate is in normal newborn babies for the first five days of the life. This is elevated when infective process is going on in neonate. Adler et al (1975) and Parida et al (1980) also observed similar findings.

Mathai et al (2004), in their study reached a conclusion that CRP level in cord blood of ≥ 6 mg/L was significantly associated with rupture of membranes for more than 24 hours, labour for more than 12 hours and maternal fever. At 24 hours, elevation in CRP levels was significantly associated with primiparity, more than three vaginal examinations after rupture of membranes, meconium staining of amniotic fluid and amnioinfusion. When the cut-off CRP level was increased to 12 mg/L, significant association was noted only with maternal fever,

Since CRP levels rise during the initial 24 hours in many babies irrespective of infection or administration of antibiotics, serial determinations in this period may not be of much use in diagnosis but may help in identifying uninfected babies and restricting antibiotic use.

In the study by Mathai et al (2004), they found at 24 hours, CRP levels of 6 mg/L had a negative predictive value of 99%. This level therefore could be used to guide antibiotic therapy when latex agglutination kits are used. Testing samples in further dilutions to establish the actual amount of CRP may not be necessary since increasing levels were not associated with increasing severity or prognosis.

In comparison to leukocyte counts and ratios, CRP levels at 24 h proved to be the single best indicator for diagnosing EOS.

Early onset pneumonia has been estimated to occur in 1.79 per 1000 live births (Webber et al 1990). Nosocomial infection causing pneumonia was found in about 8% of babies in a neonatal intensive care unit (Hemming et al, 1976). Pneumonia as a complication of endotracheal intubation for mechanical ventilation has an incidence of about 30% (Giacoia et al, 1981).

Gotoff and Behrman (1970), in their work noted an increasing trend of listeria monocytogenes infection.

Bhakoo et al (1974), Guha et al (1978), Khatua et al (1980) and Mishra et al (1985), also noted E.coli as the most common organism in the causation of neonatal infection. They also noted an increasing trend of Klebsiella infection. Other organisms reported by these workers were staph aureus, pseudomonas and peptococcus etc.

Sinha et al (1980), however, observed that P. aeuroginosa is the most common organism in the causation of neonatal sepsis (81.7%).

Mondal et al (1991), observed that staphylococcus was the most common organism in the cases who were born outside the hospital and inside the hospital. Klebsiella was more common than acinobacter among hospital born babies.

Pruthi et al (1983), in their study of 947 neonates reported that usefulness of infection scoring system at birth for predicting neonatal infections.

High risk factors are:

1. Apgar score at 1 min < 6 or frankly meconium stained liquor.
2. Foul smelling liquor at birth or gastric aspirate polymorphonuclear > 20/HPF or respiratory distress at birth.
3. Prolonged labour > 24 hours.
4. Unclean vaginal examination, maternal fever > 38^0 C within 24 hours of delivery.
5. Birth weight < 2 Kg and or gestational age < 37 weeks.
6. Leaking membranes > 24 hours.

According to a study by S. Misra et al (1991) 44 babies had pneumonia, of which 30 recovered and 14 died. There were 12 babies (28.6%) who did not have tachypnea. Seven of these non-tachypneic babies died (58.3%), while 7 out of 32 babies with tachypnea expired

(21.3%). The difference in mortality between the non-tachypneic and tachypneic babies was statistically significant) $p < 0.01$). However, 8 of these 12 babies without tachypnea were of low birth weight (75%). The mortality of low birth weight (55.6%) was significantly higher ($p < 0.01$) than the mortality of normal birth weight neonates with pneumonia (15.4%).

S. Misra et al (1991) in their study reported that at least one of the 3 rapid diagnostic tests for infection (i.e. micro-ESR more than 13 mm in first hour, absolute neutrophil count above or below the reference value for the age of the neonate and C-reactive protein positivity in the plasma by Rapi-tex) was positive in 31 babies (70.4%). Among these 31 babies a bacterial etiology of pneumonia could be established in 22 neonates (71%) by culture and CIEP (counter immuno electrophoresis) technique. Only 3 babies with positive test for bacterial infection (culture or CIEP) had all rapid diagnostic tests negative. Bacterial culture of the blood was positive in 17 babies. Gram negative and gram positive bacteria were grown from 11 and 10 babies respectively. The various bacteria isolated were Klebsiella pneumonia (5) Staph epidermis (4). Actinobacter lowfii .(3) streptococcus species (2) Pseudomonas aeruginosa (2).Coagulase negative staphylococci (1) Escherichia coli (1) Salmonella Group E (1)

Salmonella typhimurium (10) Morganella morgani (10) and Enterobacter (1).

Various investigators have used both direct and indirect methods for studying the bacteriology of neonatal pneumonia. Laryngeal / tracheal aspirates have not been shown to be useful in studying the bacterial etiology of pneumonia beyond 12h of life. Blood culture has been found useful while lung aspiration culture have been shown to be the best method. Pharyngeal - secretion and gastric aspirate culture are almost useless.

In a study by S.Thomas et al (1981) forty infants developed lobar pneumonia or bronchopneumonia. They were mostly term babies. 17 of them had prolonged rupture of membranes (PROM) for more than 24 hours while two had less than 24 hours. Of these 24 were delivered vaginally with vertex presentation and eight were delivered by lower segment caesarian section indicating that there was no significant correlation between the mode of delivery and the development of secondary pneumonia. Similarly there was no correlation between maternal illness and subsequent respiratory infection. The onset of RDS in these cases varied from 0-56 hours (mean 13.1 hr) and the maximum duration was 144 hours (mean 44.8 hr). In all these cases there was evidence of pneumonia radiologically. The organism isolated from blood culture were Klebsiella aeruginosa,

E. coli, pneumococcus staphylococcus aureus, Staphylococcus albus and salmonella typhi.

J.N Misra et al (1985) found that "Blood culture was positive in 36.4 as against 44% reported by Shakunthala et al (1978). Gram negative bacteria was detected in 11(25%) Strep. Pneumoniae antigen in 10 (22.4%) and Staph aureus in 3 (6.4%) babies". In an earlier study Shakunthala et al (1978) isolated Staph. Aureus, Strep. Pneumoniae and Gram negative bacteria from 28, 28 and 2% neonates with pneumoniae respectively. In contrast to studies from the developed countries, beta haemolytic streptococcus was not isolated from any of the cases.

Study by J.N Misra et al (1985) showed a continued high prevalence of streptococcus pneumoniae, an increasing incidence of gram negative bacteria and a falling rate of staph. aureus pneumonia. The changing bacteriology of neonatal pneumonia may be related to antibiotic usage protocol and introduction of intensive care facilities.

Among the bacterial isolates, 23.5% of the Gram negative bacteria and the staphylococci were resistant to gentamicin, while all of them were sensitive to amikacin. All the staphylococci isolated were sensitive to methicilin. Therefore initial antibiotic therapy for neonatal pneumonia should include ampicillin for streptococcal Pneumonias,

and aminoglycoside antibiotic for Gram negative bacteria (amikacin) and cloxacillin for staph. aureus.

S.Thomas et al (1981) found that the duration of onset for aspiration pneumonia was 0-11 hrs. of birth and the R.D.S. persisted for a period varying from 7-36 hours, transient tachypnea started within 0-4 hrs. and lasted for a maximum period of 48 hrs., meconium aspiration syndrome started at 0-8 hours and lasted for 62 hrs.

According to Mathur et al (2002): no significant difference was found in respiratory rate in neonates with pneumonia compared to neonates with respiratory distress due to other causes (p=0.22). Of the 103 cases with pneumonia ,11.6% neonates had respiratory rate less than 60 /min and would have been missed by the WHO definition of-pneumonia (respiratory rate greater than 60/min. The fatality in 7 neonates with respiratory rate of less than 50/min was 57.1% which .was higher than in those neonates with pneumonia having respiratory rate greater than 50/ min. Earlier studies have also found high mortality (27.7% and 58.3% respectively) in preterm neonates in whom respiratory rate was less than 50/min. In the same study by Mathur et al (2002) bacterial etiology of pneumonia was established in 49 neonates (47.5%) by blood culture. This was slightly higher than that reported earlier. The bacterial isolates are consistent with the earlier studies, which suggest increasing incidence of Klebsiella.

Following findings were established by their study "Pneumonia was the most common cause of respiratory distress in neonates. Clinical features and X-ray chest would miss the diagnosis of pneumonia in neonates in 15% cases and these have to be corroborated with sepsis screen and blood culture, for a definitive diagnosis. The diagnosis of pneumonia based on respiratory rate more than 60 per minute as suggested by WHO would miss the condition in 11.0% cases and fatality in the missed cases is higher ".

Material

&

Methods

Material and Methods

The present study was conducted in the Neonatal Intensive care unit of the Department of Pediatrics in collaboration with the department of Microbiology and Department of Pathology, M.L.B. Medical College, Jhansi. This N.I.C.U. caters to neonates delivered at home and brought directly or delivered in the college itself or referred for neonatal care from elsewhere.

CRITERIA FOR SELECTION OF CASES

Examination of Newborn

A detailed general and systemic examination of the newborn was done in each and every case. Accordingly colour, cry, activity and posture was noted. Anthropometric measurements viz. weight, head circumference, chest circumference and length of baby was also recorded.

Gestational age was assessed by Ballard's physical characteristics criteria viz. texture of hairs, ear cartilage and recoiling, size of breast nodule, scrotal rugae or position of labia majora and creases present over the sole.

Examination of head for caput or cephalhaematoma, palpation of anterior fontanelle and sutures, examination of face, oral cavity,

neck and trunk was done in each case. Due emphasis was given to observe evidence of superficial infections viz. – conjunctivitis, furunculosis, umbilical sepsis, colour of umbilical cord (meconium stained or not), jaundice and cyanosis.

Life threatening congenital anomalies and other congenital anomalies viz. choanal atresia, tracheo-oesophageal fistula, meningocele, meningomyelocele, tumour in the neck, features of Down's syndrome, congenital heart disease and renal malformations etc, were also recorded.

Systemic examination

CVS, respiratory system, examination of abdomen and complete neurological examination were done in all the newborn babies. Special emphasis was given to the character of first and second heart sounds, any murmur; or signs of congestive heart failure, enlargement of liver, spleen, kidneys or any lump in abdomen. Signs of respiratory distress viz. Respiratory rate of more than 60/minute in quiet respiration, percussion and auscultation of the chest were done to exclude any respiratory problem.

A detailed neurological examination was performed and effort was made to elicit important neonatal reflexes to assess the neurological status of the newborn.

All neonates presenting with respiratory symptoms characterized by any of the following were included in the study: (i). rapid, noisy or difficult breathing; (ii). respiratory rate > 60/min; (iii). chest retraction; (iv). cough; and (v). grunting. Surgical problems causing respiratory distress, i.e. congenital malformations affecting respiratory tract and congenital heart disease were excluded from the study.

The baby was evaluated between feeds and in quiet state. Respiratory rate was recorded for at least 1 minute. The diagnosis of respiratory problems was based on guidelines recommended by the NATIONAL NEONATOLOGY FORUM (NNF).

Pneumonia was diagnosed in the presence of respiratory distress with: (a) positive blood culture or (b) if any two of the following were present (i). existing or predisposing factors characterized by any one of the following: (a) prolonged rupture of membranes (> 24 hrs.); (ii). clinical picture of sepsis characterized by any of the following : (a) poor feeding, (b) lethargy, (c) poor reflexes, (d) hypo or hyperthermia, (e) abdominal distention; and (iii). x-ray picture suggestive of pneumonia characterized by any of the following; nodular or coarse patchy infiltrates, diffuse haziness or granularity, air bronchogram and lobar or sublobar consolidation. Transient episodes of consolidation lasting less than 48 hours due to pulmonary edema were excluded from the diagnosis of pneumonia; (iv) Positive sepsis screen.

Transient tachypnea of the newborn was diagnosed as respiratory distress in a term or borderline term neonate starting within 4 hours after birth, often requiring supplemental oxygen but recovering spontaneously within 3-4 days and showing characteristic X-ray changes, i.e. linear streaking at hilum and interlobar fluid.

Hyaline membrane disease (HMD) was diagnosed when the following three criteria are present: (a) preterm neonates; (b) respiratory distress having onset within 2 hours of birth: and (c) skiagram of chest showing poor expansion with air bronchogram or reticulogranular pattern or ground glass opacity.

Meconium aspiration syndrome was diagnosed in the presence of at least two of the following (1) meconium staining of the liquor or staining of nails or umbilical cord or skin; (2) respiratory distress soon after birth; and (3) radiological evidence of aspiration pneumonitis (atelectasis or hyperinflation).

Following investigations were done in the neonate at the time of inclusion into the study and samples, were sent to the Department of Pathology, M.L.B. Medical College, Jhansi. Sepsis screen was considered as positive if at least two of these were positive: (i) peripheral smear with bandemia more than 20%; (ii) total leukocyte count interpreted as per reference value; The total leukocyte count is usually believed to have a low predictive value for the diagnosis of

sepsis because of the wide range of normal counts from 8000 to 20,000/ cmm. Leucopenia (< 5000 /cmm) or absolute neutropenia (< 1500 /cmm) is usually associated with neonatal sepsis. A band neutrophil is an immature neutrophil, wherein the width of the narrowest segment of its nucleus is more than one third of the broadest segment.

(iii). **Micro-ESR**- interpreted as per criteria suggested earlier: and normal value is up to 6 mm in the first hour during the first 3 days of life. By the end of first month, maximum fall may be up to 11 mm during the neonatal period. A value of more than 13 mm was considered as suggestive of infection. Micro-ESR was obtained by collecting capillary blood in a standard pre-heparinized micro-hematocrit tube (75 mm length, internal diameter of 1.1 mm and outer diameter 1.5 mm) and reading the fall of erythrocyte column after one hour.

(iv) **CRP** was done by rapid slide latex agglutination method using commercial kits .These kits were available in Jhansi and a kit of 10 tests cost Rs. 350/-.

A level of more than 6 mg / L was considered as abnormal in the neonate.

Principle of the test

Rhelax CRP slide test for detection of CRP is based on the principle of agglutination. The test specimen (serum) is mixed with Rhelax CRP latex reagent and allowed to react. If CRP concentration is greater than 0.6 mg/dl a. visible agglutination is observed. If CRP concentration is less than 0.6 mg/dl, then no agglutination is observed.

Required Testing Material

1. Rhelax CRP reagent: A uniform suspension of polystyrene latex particles coated with Anti-CRP antibodies (Monoclonal IgG).
2. Positive control, reactive with Rhelax CRP reagent.
3. Negative control, non-reactive with Rhelax CRP reagent. The Rhelax CRP reagent is standardized to detect CRP concentrations greater than 0.6 mg/dl.
4. Glass slide with six reaction circles
5. Sample dispensing pipettes, Mixing sticks, Rubber teat.
6. Stop watch, Test tuber, a high intensity direct light source, isotonic saline.

Specimen Collection and Storage

The samples were withdrawn within few hours of admission and serum separated after centrifugation simultaneously in the ward itself.

Fresh sera/ Plasma was used for the test. Usual precautions for venepuncture were observed. No sample pretreatment was necessary, so none were taken.

The reagent was stored at 2 - 8°C and not frozen.

1. Markedly lipemic, hemolysed and contaminated serum samples could produce non-specific results.
2. Use of plasma rather than serum can lead to false positive results.
3. Do not read results beyond indicated testing time limits.

Test Procedure

Both reagents and samples were brought to room temperature before use.

Semi quantitative method

1. Using isotonic saline prepare serial dilutions of the serum sample 1:2,1:4, 1:8, 1:16,1:32,1:64 and so on.
2. Pipette each dilution of the serum sample onto separate reaction circles.
3. Add one drop of Rhelax CRP latex reagent to the drop of test specimen on the slider. Do not let the dropper tip touch the liquid on the slide.
4. Using a mixing stick, mix the sample and the latex reagent uniformly over the entire circle.

5. A stopwatch was started immediately and the slide was rocked gently, back and forth, observing for agglutination macroscopically at two minutes.

INTERPRETATION OF RESULTS

Semi quantitative method

Agglutination in the highest serum dilution corresponded to the approximate amount of CRP in mg/dl present in the specimen. Concentration of CRP was calculated as follows:

CRP (mg / dl) = 0.6 x D

Where D = highest dilution of serum showing agglutination.

All bacterial isolates were identified by conventional methods, X-ray chest was interpreted as per suggested criteria. Blood from radial or posterior tibial artery was taken by complete aseptic precaution in a 1ml syringe after heparinizing by a sterile concentrated heparin solution. Arterial line was used whenever available. Care was taken to ensure that the baby is not crying.

The samples for blood culture were isolated by standard methods and were sent to the Department of Microbiology M.L.B. Medical College, Jhansi. Samples, for testing the drug sensitivity of the prevalent bacteria, isolated from blood culture positive cases was done by KIRBY BAUER Method.

Observations

Observations

The present study was conducted on 50 neonates, admitted in the NICU of Department of Pediatrics M.L.B. Medical College, Jhansi from November 2003 to October 2004.

The present study comprised of neonates presenting with respiratory distress delivered in the Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi and elsewhere, but admitted in our NICU. The study was conducted on the spectrum of respiratory distress, signs and symptoms, clinical history and investigations suggestive of four diseases, i.e. Pneumonia, Transient tachypnoea of the newborn, Hyaline membrane disease (HMD), Meconium aspiration syndrome (MAS).

Table 1

Spectrum of Respiratory Distress in neonates

Study group	No. of total cases	
	(n= 50)	%
Pneumonia	23	46
Hyaline membrane disease (HMD)	21	42
Meconium aspiration syndrome (MAS)	4	8
Transient tachypnoea of the newborn (TTNB)	2	4
Total	50	100

Table 1 shows the various study groups, their number and percentage that we witnessed amongst the neonates brought to our

NICU with respiratory distress. In the present study, pneumonia was found to be the most common cause of respiratory distress in neonates (46%), followed by HMD (42%), meconium aspiration syndrome (8%) while TTNB was found in 4% cases.

Table 2

Number and percentage distribution of RDS cases amongst total admissions in NICU (November'03 to October '04)

	Number of cases with RDS	Percentage
Total admissions in NICU (n = 168)	50	29.76
Total fatality in NICU (n=73)	21	28.7%

Table 2 shows the percentage contribution of respiratory distress amongst admissions in our NICU. This table reveals that respiratory distress was responsible for 29.76% cases admitted in our NICU.

Table 3

Sex wise distribution of the neonates

Study group	Male	Female	Ratio
Pneumonia	17	6	2.8 : 1
Transient tachypnoea of the newborn (TTNB)	2	0	2 : 0
Meconium aspiration syndrome (MAS)	3	1	3 : 1
Hyaline membrane disease (HMD)	13	8	1.6 : 1
Total	35	15	2.3 : 1

Table 3 depicts the sex wise distribution of cases. Exclusively males were found to have transient tachypnea of newborn. In hyaline membrane disease males were affected 1.6 times more than their

female counterparts. In MAS the male female ratio was 3:1. Pneumonia was also very sinister in causing distress in 2.8 males for every female.

This table is significant in the fact that given the same birth condition males were more predisposed to developing respiratory distress.

The total male: female ratio was 2.3 : 1 which indicates the vulnerability of the male sex to respiratory distress amongst the neonates.

Table 4

Birth weight and gestational age in various study groups

Study material		Pneumonia No. (%)	HMD No. (%)	MAS No. (%)	TTNB No. (%)
Birth weight	1 – 1.4 Kg	2 (8.7%)	9 (42.9%)	0	0
	1.5– 1.9 Kg	2 (8.7%)	9 (42.9%)	0	0
	2 – 2.4 Kg	6 (26.1%)	3 (14.2%)	0	0
	> 2.5 Kg	13 (56%)	0	4 (100%)	2 (10%)
Mean birth weight		2.20 Kg	1.4 Kg	3.08 Kg	2.6 Kg
Gestational age	< 34 weeks	2 (8.7%)	21 (100%)	0	0
	34 – 37 weeks	7 (30.4%)	0	0	0
	37 – 42 weeks	14 (60.9%)	0	2 (50%)	2 (100%)
	> 42 weeks	0	0	2 (50%)	0

Table 4 shows the distribution of birth weights and gestational ages of neonates in various study groups. It is evident from the table, that 40% of neonates with pneumonia were low birth weight, and one was small for gestational age. 7 neonates did not complete 37 weeks of gestation and were born prematurely. So, 14 (60%) of our cases

developing pneumonia were fullterm, while nine (40%) were preterms in this study.

While, in HMD 100% neonates were low birth weight, 85.8% were < 2000 gms and all the 21 cases of HMD were premature (< 34 weeks). In MAS and TTNB none of the babies were of low birth weight or premature.

Table 5

Comparative table of various signs and symptoms and their number and percentage wise occurrence in study group

Signs and symptoms	Pneumonia No. (%)	HMD No. (%)	MAS No. (%)	TTNB No. (%)
	(n = 23)	(n = 21)	(n = 4)	(n = 2)
Respiratory rate > 60/min	21 (91.3%)	19 (90.47%)	4 (100%)	2 (100%)
Difficulty in feeding	22 (95.6%)	18 (85.7%)	4 (100%)	1 (50%)
Flaring of alae nasi	23 (100%)	20 (95.2%)	3 (75%)	1 (50%)
Chest retractions	20 (86.9%)	18 (85.7%)	3 (75%)	1 (50%)
Adventitious sounds	8 (34.8%)	2 (9.5%)	1 (25%)	0
Cyanosis	8 (34.7%)	3 (14.3%)	1 (25%)	0
Cough	4 (17%)	0	0	0

Table 5 compares the number and percentage occurrence of various signs and symptoms in the study group. RR > 60 / minute difficulty in feeding, flaring of alae nasi and chest retractions had maximum incidence in all the four groups, while cyanosis and cough were most specific for pneumonia only. Adventitious sound on chest auscultation were found in maximum number (34.8%) in the cases belonging to pneumonia.

Table 6

Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing neonatal pneumonia

Signs and symptoms	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Flaring of alae nasi (n = 23)	100	7.4	47.9	100
Difficulty in feeding (n = 22)	95.6	11	47.8	75
Respiratory rate >60/min (n = 21)	91.3	7	45.6	50
Chest retractions (n = 20)	86.9	18.5	47.6	62.5
Adventitious sounds (n = 8)	34.8	88.8	72.7	61.5
Cyanosis (n = 8)	34.7	85	66.6	60.5
Cough (n = 4)	17	100	100	58.7

Table 6 shows the Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing neonatal pneumonia. Cough, adventitious sounds and cyanosis had high specificity in diagnosing neonatal pneumonia, while difficulty in feeding, RR > 60 , flaring of alae nasi and chest retractions had high sensitivity for diagnosing pneumonia. There were 2 babies who did not have tachypnoea. Both these babies expired.

Table 7

Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Transient tachypnea of the newborn

Signs and symptoms	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Respiratory rate > 60/min (n = 2)	-	8.3	4.3	100
Difficulty in feeding (n = 1)	50	4	2	66.6
Chest retractions (n = 1)	50	14.5	2	87.5
Flaring of alae nasi (n = 1)	50	2.1	2	50
Cyanosis (n = 0)	-	75	-	94.7
Cough (n = 0)	-	91.6	-	95.6
Adventitious sounds (n = 0)	-	77	-	94.9

This table was planned to evaluate the sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Transient tachypnea of the newborn. No strong association was found with any of the factors enumerated in the table. Although, absence of cough and absence of adventitious sounds, were highly specific for TTNB, no conclusive evidence could be drawn as our sample size was too small (n=2).

Table 8

Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Meconium aspiration syndrome

Signs and symptoms	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Difficulty in feeding (n = 4)	-	6.5	8.5	100
Respiratory rate > 60/min (n = 4)	-	8.6	8.6	100
Chest retractions (n = 3)	75	15.2	7.1	87.5
Flaring of alae nasi (n = 3)	75	2.2	6.25	50
Adventitious sounds (n = 1)	25	78.2	9	92.3
Cyanosis (n = 1)	25	76	8.3	94.5
Cough (n = 0)	-	92	-	91.3

This table was planned to evaluate the Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Meconium aspiration syndrome. Apart from the absence of cough and adventitious sounds, which have a high specificity, no other factor had any conclusive data to be of any use. Only one case amongst meconium aspiration syndrome had cyanosis in our study.

Table 9

Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Hyaline membrane disease

Signs and symptoms	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Flaring of alae nasi (n = 20)	95.2	3.4	41.6	50
Respiratory rate >60/min (n = 19)	90.47	6.8	41	50
Chest retractions (n = 18)	85.7	17.2	42.9	52.5
Difficulty in feeding (n = 18)	85.7	6.9	40	40
Cyanosis (n = 3)	14.3	68.9	25	52.6
Adventitious sounds (n = 2)	9.2	68.9	18.18	51.2
Cough (n = 0)	-	86	-	51

This table evaluates the Sensitivity, specificity and predictive value of clinical signs and symptoms in diagnosing Hyaline membrane disease. Absence of cough and adventitious sounds was specific in cases of HMD. Remaining factors had a high sensitivity, but were too frequent in other study groups also, so no conclusive evidence could be derived.

Table 10

Comparative table of antenatal, natal and post natal history and their no. and percentage wise incidence in study groups

Antenatal History	Pneumonia	HMD	MAS	TTNB
	No. (%)	No. (%)	No. (%)	No. (%)
1. Maternal fever > 38°C	2 (8.61%)	2 (9.5%)	Nil	Nil
2. Prolonged Rupture of membranes > 24 hrs	10 (43.4%)	5 (23.8%)	Nil	Nil
3. Leaking per vaginum	6 (26.1%)	5 (23.8%)	Nil	Nil
4. Foul smelling liquor	2 (8.6%)	0	Nil	Nil
5. H/o diabetes in mother	0	0	Nil	Nil
6. H/o fetal distress	0	0	3 (75%)	Nil

Natal History	Pneumonia	HMD	MAS	TTNB
	No. (%)	No. (%)	No. (%)	No. (%)
1. H/o prolonged labour	4 (17.3%)	Nil	3 (75%)	Nil
2. H/o precipitate labour	Nil	Nil	Nil	Nil
3. Traumatic Labour (Obstetrical accident)	Nil	Nil	Nil	Nil
4. H/o poor cry / resuscitation	Nil	Nil	3 (75%)	Nil

Post Natal History	Pneumonia	HMD	MAS	TTNB
	No. (%)	No. (%)	No. (%)	No. (%)
1. Meconium staining of Liquor /cord /Nails /Skin	Nil	Nil	4 (100%)	Nil
2. Difficulty in feeding	22 (95.6%)	18 (85.7%)	4 (100%)	1 (50%)
3. Fever	6 (35.3%)	Nil	Nil	Nil
4. Weight < 2000 gms.	4 (17.3%)	18 (85.7%)	Nil	Nil
5. Gestation < 34 weeks	2 (8.7%)	21 (100%)	Nil	Nil
Post mature	Nil	Nil	2 (50%)	Nil

Table 10 of antenatal history highlights prolonged rupture of membranes in mothers, as the most important factor responsible for pneumonia in neonates. A small majority of mothers whose neonates developed HMD, also had history of PROM and leaking per vaginum. That could be because, both rupture of membranes and leaking per vaginum in itself can lead to preterm labour and birth. A history of fetal

distress leading to emergency LSCS was found in 75% cases of meconium aspiration syndrome.

Table 10 of natal history reveals that prolonged labour and a history of poor cry were both found in 75% cases of MAS. History of prolonged labour in a small majority (17.3%) was also present in neonates developing pneumonia. In rest of the disorders neither prolonged / precipitate / traumatic labour was found.

Table 10 of post natal history reveals that meconium staining of liquor was found in all the four cases of MAS. A history of difficulty in feeding and fever at the time of admission was found in maximum number of cases (22), (6) respectively with pneumonia. None of the other disorders had fever at the time of admission. All the neonates developing HMD (n = 21) were preterm and 18 (85.7%) were < 2 Kg. The remaining 3 babies developing HMD were of 2 Kg birth weight. Difficulty in feeding was found in 85.7% cases of HMD also. 50% of neonates with MAS were post mature and all the four neonates had difficulty in feeding. Only one neonate of TTNB out of two admissions had problem in feeding.

Table 11

Sensitivity, specificity and predictive value of Antenatal history in diagnosing Pneumonia in neonates with Respiratory distress

Antenatal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Leaking per vaginum (n = 6)	26.1	81.5	54.5	56.4
Foul smelling liquor (n = 2)	8.6	96.2	66.6	56
Maternal fever (n = 2)	8.61	88.8	40	53.3
Prolonged rupture of membranes >24h (n = 0)	43.4	81.4	66.6	62.8

Table 11 shows the incidence of various antenatal factors presumed to be responsible for pneumonia in neonates. Eleven mothers of neonates with respiratory distress had predisposing factors for pneumonia. These factors have high specificity and positive predictive value, but poor sensitivity. Maternal fever and foul smelling liquor have highest specificity followed by PRM and leaking per vaginum.

None of the factors like maternal fever, prolonged rupture membranes, leaking per vaginum or foul smelling liquor was found to have any association at all with transient tachypnea of newborn (TTNB).

Table 12

Sensitivity, specificity and predictive value of Antenatal history in diagnosing neonates with Meconium aspiration syndrome

Antenatal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
History of fetal distress (n = 3)	75.1	97.3	75.1	97.8

Except for a history of fetal distress, none of the factors enumerated in antenatal history like PRM, maternal fever, LPV had any association at all with meconium aspiration syndrome (MAS).

Fetal distress had a high specificity and negative predictive value for MAS.

Table 13

Sensitivity, specificity and predictive value of Antenatal history in diagnosing neonates with Hyaline membrane disease

Antenatal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Prolonged rupture of membranes >24h (n = 5)	23.8	65.5	33.3	54.2
Leaking per vaginum (n = 5)	23.8	79.3	45.4	58.5
Maternal fever (n =2)	9.5	89.6	40.1	57.8
Foul smelling liquor (n = 0)	-	-	-	-

This table highlights the antenatal factors like maternal fever, PRM, and LPV, and their association with HMD. All these factors had a high specificity for HMD, probable explanation could be that these factors were indirectly also responsible for preterm labour and birth.

Table 14

Sensitivity, specificity and predictive value of Natal history in diagnosing Pneumonia in neonates with Respiratory distress

Natal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
H/O prolonged labour (n = 4)	17.3	88.8	57	55.8
H/O precipitate labour (n = 0)	-	-	-	-
Traumatic labour/obstetrical accident (n = 0)	-	-	-	-
H/O poor cry / resuscitation (n = 0)	-	-	-	-

Table 14 shows that prolonged labour is the only natal factor (amongst other factors enumerated in the table) which was found to have a high specificity (88.8%) for neonates having pneumonia. Others failed to show any association at all in our study.

Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with TTNB.

Table 15

Sensitivity, specificity and predictive value of Natal history in diagnosing neonates with Meconium aspiration syndrome

Natal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
H/O prolonged labour (n = 3)	75	91.3	42.9	97.6
H/O precipitate labour (n = 0)	-	-	-	-
Traumatic labour/obstetrical accident (n = 0)	-	-	-	-
H/O poor cry / resuscitation (n = 3)	75	100	100	97.8

A history of prolonged labour and a history of poor cry or resuscitation in newborn have a high specificity for MAS. History of poor cry in natal history had a 100% positive predictive value (PPV) for neonates developing respiratory distress due to MAS. We could not find

any cases of precipitate or traumatic labour leading to MAS, so no association could be established.

Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with HMD.

Table 16

Comparison between various diseases according to mode of delivery

Mode of delivery	Hyaline Membrane Disease	Meconium Aspiration Syndrome	Transient Tachypnea of the newborn	Pneumonia
Emg. LSCS	11 (52.4%)	3 (75%)	2 (100%)	9 (39.1%)
Vaginal delivery	10 (47.6%)	1 (25%)	0	14 (60.9%)

Table 16 compares the mode of delivery and its association, if any, to the occurrence of above mentioned disorders. A slightly higher percentage of cases delivered by emergency LSCS developed HMD, while 60.9% cases delivered per vaginally developed pneumonia. This could be explained by a sizable majority of deliveries being conducted at home, in the latter (n = 14).

Table 17

Comparison between various diseases according to place of delivery

Place of delivery	Hyaline Membrane Disease	Meconium Aspiration Syndrome	Transient Tachypnea of the newborn	Pneumonia
Hospital	18 (85.7%)	3 (75%)	2 (100%)	13 (56.5%)
Outside by untrained dai	3 (14.28%)	1 (25%)	0	10 (43.5%)

Table 17 compares the places of delivery and the occurrence of various disorders accordingly. Twenty eight percent of all the neonates with respiratory distress were delivered at home. 43.5% cases of

pneumonia were delivered at home. 18 cases of HMD were delivered in hospital, because most of them had to be delivered by emergency LSCS. There were 5 twins in our study, which was in itself a high risk delivery.

Table 18

Sensitivity, specificity and predictive value of post-natal history in diagnosing neonates with Pneumonia

Post-natal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Difficulty in feeding (n = 22)	95.6	11	47.8	75
Fever (n = 6)	35.3	100	100	61.4
Weight < 2000 gms (n = 4)	13.1	33.3	14.3	31
Gestation < 34 wks (n = 2)	8.7	22.2	8.7	22.2
Post mature (n = 0)	-	92.5	-	52.1
Meconium staining of liquor /cord /nails /skin (n = 0)	-	85.2	-	50

Duration of onset of respiratory distress 0 – 15 hours (n = 11) 47.8% cases.

A history of difficulty in feeding in the post natal period with fever had a high specificity for diagnosing pneumonia. Fever and post maturity also had a high specificity, but low sensitivity, 0% in the case of post maturity. 47.8% of cases had an onset of respiratory distress within 15 hours of birth and were later diagnosed as pneumonia. 9 of the newborns having pneumonia in our study were preterms, only 2 were less than 34 weeks gestational age.

Apart from a difficulty in feeding (50%), none of the other post natal factor could be associated with TTNB.

100% cases later diagnosed as TTNB presented with respiratory distress within 4 hours of birth.

Table 19

Sensitivity, specificity and predictive value of post-natal history in diagnosing neonates with Meconium aspiration syndrome

Post-natal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Meconium staining of liquor / cord/ nails /skin (n = 4)	100	100	100	100
Difficulty in feeding (n = 4)	100	89.1	44.4	100
Fever (n = 0)	-	-	-	-
Weight < 2000 gms (n = 0)	-	-	-	-
Gestation < 34 wks (n = 0)	-	-	-	-
Post mature (n = 2)	50	100	100	95.8

Duration of onset of respiratory distress 0 – 8 hours (n = 3) (75%) cases.

Table 19 shows that meconium staining of cord, liquor and nails had a 100% sensitivity, specificity and predictive value for MAS. Post maturity also had a 100% specificity and positive predictive value in cases diagnosed as MAS. None of the cases had fever at the time of admission, or were premature.

Table 20

Sensitivity, specificity and predictive value of post-natal history in diagnosing neonates with Hyaline membrane disease [n = 21]

Post-natal history	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Gestation < 34 wks (n = 21)	100	93.1	91.3	100
Difficulty in feeding (n = 18)	85.7	6.8	40	40
Weight < 2000 gms (n = 18)	85.7	89.6	85.7	89.6
Post mature (n = 0)	-	-	-	-
Fever (n = 0)	-	-	-	-
Meconium staining of liquor / cord/ nails / skin (n = 0)	-	-	-	-

Duration of onset of respiratory distress 0 – 6 hours (n = 15) (71.4%) cases.

Table 20 aims to evaluate the various post natal factors for their Sensitivity, specificity and predictive value in diagnosing HMD. As is evident from the chart that weight and gestational age have the highest sensitivity, specificity and NPV for diagnosing HMD. None of the cases with HMD had fever or meconium staining.

Table 21

Investigations used to diagnose pneumonia in 23 neonates

Investigations	No. (cases)	%
Blood culture positive and chest x-ray positive (Sepsis screen positive in 6 cases)	9	39.1
Blood culture no growth but chest x-ray positive (Sepsis screen positive in 4 cases)	8	34.8
Blood culture positive but chest x-ray clear (Sepsis screen positive in 2 cases)	4	17.4
Blood culture no growth and chest x-ray bilateral clear but Sepsis screen positive	2	8.7
Totals	23	100

Out of 23 cases of pneumonia, blood culture was positive in 13 cases (56.5%), chest x-ray was positive in 17 cases. Both blood culture and chest x-ray were positive in 39.2% of cases. In 8.7% of the cases only sepsis screen was found to be positive. Sepsis screen was positive in 14 cases along with other investigations in pneumonia. Amongst these 14 cases, a bacterial etiology of pneumonia could be established in 92% 13 cases by blood culture.

In the present study, definitive pneumonia (blood culture positive) cases were 39.1%, while cases belonging to probable pneumonia (blood culture negative, chest x-ray positive) were 34.8% only.

Amongst 17 x-ray chest positive cases in pneumonia, 11 cases showed alveolar infiltrates (47.8%), 4 cases showed diffuse haziness (17.3%), 2 cases showed lobar consolidation (8.6%), while 6 cases had chest x-ray clear (26.1%).

X-ray chest was positive in 50% cases of TTNB. Chest x-ray showed changes pertaining to MAS in 50% cases. In HMD, only 33.3%

cases turned out to be chest x-ray positive. Rest other investigations were negative in all these three diseases i.e. HMD, TTNB, MAS and diagnosis was aided by clinical history and examination.

Table 22

Distribution of positive cases of various investigations amongst the spectrum of respiratory distress

Investigations		Pneumonia (n = 23)	HMD (n = 21)	MAS (n = 4)	TTNB (n = 2)
		No. (%)	No. (%)	No. (%)	No. (%)
	1 – 6 mm	9 (39%)	18 (85%)	2 (50%)	2 (100%)
Micro-ESR	7 – 12 mm	8 (34%)	3 (14%)	0	0
	13 – 20 mm	6 (26%)	0	0	0
CRP positive		14 (60%)	2 (9%)	1 (25%)	0
Blood culture		13 (56%)	0	0	0
Band cells	0 – 10%	11 (47%)	21 (100%)	4 (100%)	2 (100%)
	10 – 20%	9 (39%)	0	0	0
	20 – 30%	3 (13%)	0	0	0

Table 22 was planned to give an idea of the results of various investigations we did throughout our study. It highlights the number of positive cases of the investigations amongst the study group.

Micro-ESR, blood culture and band cells were positive exclusively in cases of pneumonia. Maximum cases of CRP positive belong to pneumonia except for two cases in HMD and one case of MAS.

Table 23

Sensitivity, specificity and predictive value of various investigations in diagnosing neonates with pneumonia

Investigation	Total		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	No	%				
Blood culture positive	13	56.5	56.5	100	100	72.9
CRP positive (> 0.6 mg/dl)	14	60	60	92.6	87.5	73.5
M- ESR positive (> 13 mm)	6	26	26	100	100	61.4
Band cells (>20%) & toxic granules	3	13	13	100	100	57.4

Table 23 evaluates the sensitivity, specificity and predictive value of various investigations in diagnosing neonates with pneumonia. Though sepsis screen parameters had a high specificity above 90%, the sensitivity was low. It is 60% for CRP, 26% for micro-ESR and 13% for band cells. Blood culture had a high sensitivity of 56.5% and a 100% positive predictive value in diagnosis of neonates with pneumonia.

Table 24

Association of risk factors with CRP

Risk factor	Number of cases observed	CRP positive cases	Percentage (%)
Prolonged rupture membranes >24 hrs	10	6	60 (%)
Maternal fever	2	1	50 (%)
Leaking per vaginum	6	2	33 (%)
Foul smelling liquor	4	1	50 (%)

Table 24 shows the percentage positivity of CRP in cases having predisposing factors for pneumonia. It was meant to evaluate the association of risk factors, CRP and pneumonia. CRP was found to be

positive in 60% cases of prolonged rupture of membranes, which later developed into cases of pneumonia in our study.

Table 25

Percentage of low birth weight (< 2.5 Kg) deaths amongst total fatality due to particular respiratory disease

Study group	Total no. of cases	No. & % of LBW cases	Total no. of deaths	No. & % fatality in fullterms	No. & % fatality in LBW cases
Pneumonia	23	10 (43.4%)	7	3 (42.9%)	4 (57.1%)
HMD	21	21 (100%)	11	0	11 (52.4%)

This table indicates the percentage significance of low birth weight responsible for deaths amongst total fatality due to a particular disease. Out of 23 cases of pneumonia 7 neonates expired. Out of these 7 neonates which expired because of pneumonia, 4 babies were of low birth weight i.e. < 2500 gms, showing 57.1% mortality rate. Amongst these 4 deaths 2 fatalities were those who did not have tachypnoea (RR > 60) on physical examination. Both of them 100% expired making the difference in mortality between tachypnoeic and non- tachypnoeic babies statistically significant. In HMD, 52.4% mortality was found in low birth weight section.

Table 26

Fatality in neonates with Respiratory Distress

Study group	Fatality	
	(n=21)	%
Pneumonia (n = 23)	7	30.43
Hyaline membrane disease (HMD) (n = 21)	11	52.38
Meconium aspiration syndrome (MAS) (n = 4)	3	75.00
Transient tachypnea of the newborn (TTNB) (n = 2)	0	0.00
Total	21	-

The overall mortality rate in the present study was 42% in neonates diagnosed to be having respiratory distress. Cases belonging to meconium aspiration syndrome had the highest fatality (75%) followed by HMD ranking second (52.38%) and in pneumonia (30.43%).

Table 27

Number and percentage of morbidity and mortality of twin deliveries having Hyaline Membrane Disease

No. of twin deliveries		1st twin expired		2nd twin expired	
No.	%	No.	%	No.	%
5	100	2	40	3	60

In our study of 5 twin deliveries developing HMD, three second twin deliveries expired as compared to only 2 first twin deliveries.

Table 28

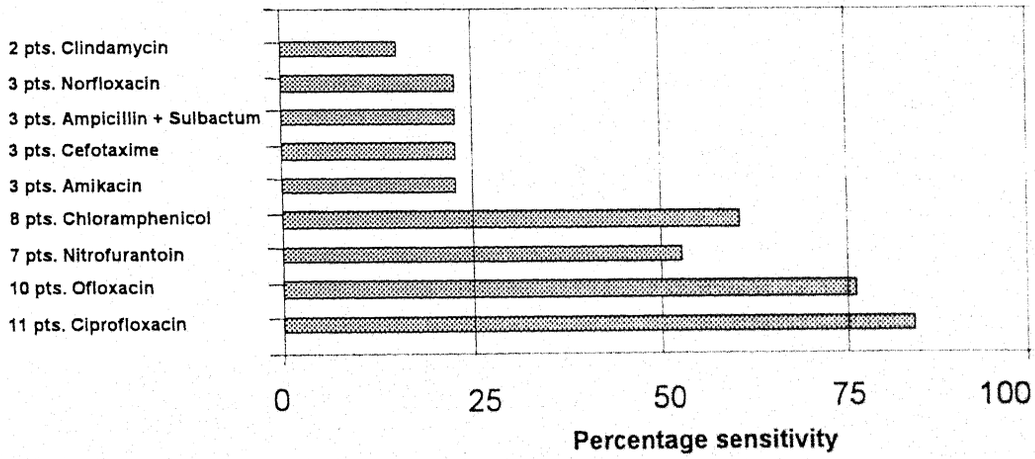
Most common organism found in blood culture positive cases

Isolate	Number of blood culture positive cases	% of blood culture positive cases
Klebsiella	8	61.5
S. aureus	2	15.4
E. coli	3	23.1
Total	13	100

Table 28 shows the most common organism found in blood culture positive cases. Out of 13 blood culture positive cases, 8 were isolated as of Klebsiella (61.5%), 3 were E.coli (23.1%) and 2 were of staph. Aureus (15.4%). Klebsiella was the major isolate in cases belonging to pneumonia.

Table 29

Bacteriological sensitivity pattern found in blood culture positive cases



Amongst the various antibiotics depicted in the chart, Ciprofloxacin and Ofloxacin, followed by Chloramphenicol were sensitive in 84.62%, 76.92%, and 61.54% cases of pneumonia respectively. Other drugs like Ampicillin + sulbactum, Amikacin, Cefotaxime and Norfloxacin were effective in only 23.08% cases each.

Discussion

Discussion

The present study was conducted on 50 neonates, admitted in NICU of the Department of Pediatrics, M.L.B. Medical College, Jhansi from November 2003 to September 2004, with respiratory distress. The present study was undertaken with the following aims:

1. To find the causes of respiratory distress in neonates brought to our Neonatal Intensive Care unit with symptoms suggestive of respiratory disorder.
2. To evaluate clinical signs like cough, difficulty in feeding, cyanosis, respiratory rate, chest retractions, flaring of alae nasi and adventitious sounds for diagnosis of neonatal pneumonia.
3. Determine bacterial etiology of neonatal pneumonia.
4. To study the sensitivity pattern of the prevalent bacteria in neonatal intensive care unit.

Incidence of spectrum of Respiratory distress disorders

It was our endeavor to explore the spectrum of respiratory distress in neonates encompassing four disorders namely : Pneumonia, HMD, MAS and TTNB. In our study, pneumonia was the leading cause of respiratory distress with incidence 46%, followed by HMD 42%, MAS 8%, and TTNB 4% respectively. Respiratory distress

forms 30% of all the admissions to our NICU. Studies in the past by Shaffer et al, had found RDS as the leading cause in premature and massive aspiration in full term with pneumonia as second. Cunnigham and Smith attributed the respiratory distress as belonging to RDS 75% and massive aspiration as 23%. SP Khatua (1979), reported highest incidence of aspiration syndrome (57.1%), followed by pneumonia 9.35% and RDS 8.8%. S.Thomas et al, found pneumonia in 44% of cases as a leading disorder with TTNB in 19.2%, MAS in 12.2% and HMD in 8.6%. Mathur et al (2002), also found in his study that pneumonia was the most common cause of respiratory distress in neonates. He reported the incidence to be 68.7%, other disorders were as follows – HMD (4%), MAS (4%), TTNB (7.33%).

The admission figures are in close similarity to the study by NB Mathur et al, where they are 29.2% of all admissions.

In our study the male : female ratio of neonates developing respiratory distress was 2.3 : 1. Males were 1.6 times more predisposed than the females in hyaline membrane disease. Pneumonia and MAS affected approximately 3 males for every female in our study. Driscoll and Smith (1962), found the male : female ratio as 2:1. S.P. Khatua found that the male : female ratio was 1.94 : 1.

Birth weights and gestational ages of neonates in various study groups

It is evident from table 4 that 40% of neonates with pneumonia were low birth weight, and one was small for gestational age. 7 neonates did not complete 37 weeks of gestation and were born prematurely. So, 14 (60%) of our cases developing pneumonia were fullterm, while nine (40%) were preterms in this study.

While, in HMD 100% neonates were low birth weight, 85.8% were < 2000 gms and all the 21 cases of HMD were premature (< 34 weeks). In MAS and TTNB none of the babies were of low birth weight or premature.

The mean birth weight for neonates developing pneumonia was 2.2 Kg, 1.4 Kg for HMD, 3.02 Kg for MAS and 2.6 Kgs for TTNB.

Authors like SP Khatua et al (1979), JN Mishra (1985), S Mishra (1991) and NB Mathur (2002) had mentioned separately the significance of low birth weight and its contribution to mortality and morbidity with respect to various respiratory distress disorders.

In the study by SP Khatua et al (1979), 30.45% cases with respiratory distress were premature and 53.7% were fullterm. In the study by S. Thomas et al (1981), they found a higher percentage of preterms developing respiratory distress. In their study they found that

out of 51 cases of pneumonia 26 were preterm. In the study by NB Mathur et al (2002), 48% of neonates with pneumonia were preterm.

Clinical signs and symptoms

Most of the neonates in our study were admitted with signs of respiratory distress, but we found few signs more specific for one disease and few signs more sensitive for the others. Table 5 of our study compares the number and percentage occurrence of various signs and symptoms in the study group. RR > 60 / minute difficulty in feeding, flaring of alae nasi and chest retractions had maximum incidence in all the four groups, while cyanosis and cough were most specific for pneumonia only. Adventitious sound on chest auscultation were found in maximum number (34.8%) in the cases belonging to pneumonia.

In our study we found cough, adventitious sounds & cyanosis had high specificity (100%), (88.8%) and (85%) respectively in diagnosing neonatal pneumonia. Difficulty in feeding, RR > 60 , flaring of alae nasi and chest retractions had high sensitivity (95.6%), (91.3%), (100%) and (86.9%) respectively for diagnosing pneumonia (Table 6). In the study by NB Mathur et al, cough, adventitious sounds, and flaring of alae nasi had high specificity which were (100%), (91.4%) and (70.2%) respectively. Chest retractions, difficulty

in feeding and RR > 60 / minute had high sensitivity (> 88%) for diagnosis of pneumonia in neonates.

In our study, of 23 cases of pneumonia, we found two cases with RR < 60 (8.7%), both of them had gestational age < 34 weeks and weight < 2 Kg, but the mortality was 100%. Thus, 100% mortality in non-tachypnoeic babies in our study was basically correlated to low birth weight and prematurity.

It was first pointed out by Mishra et al (1985), that the mortality in non-tachypnoeic as compared to tachypnoeic cases was significant. He found that out of 12 non-tachypnoeic babies, 7 died which was 58.3% mortality, while only 7 out of 32 with tachypnoea expired (21.31%). Further, he discovered one of the important correlate of low birth weight with non-tachypnoeic neonates. This was further substantiated by Mathur et al, who found 11.6% neonates had respiratory rate < 60/minute and found that the mortality increased even more (57.1%) when the RR was less than 50. In his study, out of 12 neonates having RR < 60/minute 5 expired, 7 had gestational age < 34 weeks and birth weight < 1800 gms.

Antenatal history

In our study, (Table 11) 11 mothers had factors like history of PRM (10), maternal fever (2), leaking per vaginum predisposing to

pneumonia. These factors like the study by Mathur et al had high specificity (> 80%) and positive predictive value. In his study on the spectrum of respiratory distress disorders in neonates, SP Khatua (1979), took similar parameters to aid antenatal diagnosis of pneumonia like the ones in our study. According to him out of 17 cases of pneumonia, 2 had history of prolonged rupture membranes (PRM) in mothers. In the study by S Thomas et al (1981), out of 40 infants of pneumonia, 17 mothers had history of PRM for > 24 hours and 2 had history of PRM for < 24 hours. In a study by NB Mathur (2002), out of 103 cases of pneumonia 35 mothers had prolonged rupture of membranes. In the same study, 21 mothers had history of recent febrile illness around labour. All in all the study by Mathur et al, 42 mothers had predisposing factors for pneumonia.

None of the factors like maternal fever, prolonged rupture membranes, leaking per vaginum or foul smelling liquor was found to have any association at all with transient tachypnoea of newborn (TTNB).

Except for a history of fetal distress, none of the factors enumerated in antenatal history like PRM, maternal fever, LPV had any association at all with meconium aspiration syndrome (MAS) (Table 12).

Fetal distress had a high specificity and negative predictive value for MAS.

SP Khatua et al (1979), found the highest incidence of aspiration syndrome in their study and in retrospect found that such mothers had poor antenatal check-up history and history of fetal distress (n = 64) too.

S Thomas et al (1981), like in our study could not find any association between PRM and MAS.

The most unprecedented finding while calculating for observations (Table 13) for ANH (antenatal history) in diagnosing neonates with HMD was the high incidence of prolonged rupture membranes (PRM) and leaking per vaginum (L P/V) in mothers of such neonates. No earlier study has ever mentioned these findings, so no comparison was available. In our study, 5 mothers of neonates with HMD had PRM and 5 had L P/V. Probable explanation could be that these factors were indirectly also responsible for preterm labour and birth.

Natal history

In our study (Table 14), we found that prolonged labour was the only natal factor which was found to have a high specificity (88.8%) for neonates having pneumonia. Other factors like precipitate / traumatic

labour or a history of poor cry failed to show any association at all in our study regarding pneumonia.

SP Khatua et al, found that 15 out of 17 cases of pneumonia in his study also had a history of prolonged labour. NB Mathur et al, had not done any study regarding the natal study of pneumonia. Bhakoo et al in their study on septicemia had given a high risk score of 2 for septicemia if it had a history of PRM, but had not mentioned any cases.

Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with TTNB in our study.

In the present study, prolonged labour and a history of poor cry or resuscitation in newborn have a high specificity (91.3%) and (100%) respectively for MAS (Table 15). History of poor cry in natal history had a 100% positive predictive value (PPV) for neonates developing respiratory distress due to MAS. This study is substantiated by the study of SP Khatua et al (1979), who found that out of 104 cases of aspiration syndrome, 64 infants had abnormal delivery due to fetal distress, prolonged labour, failed medical induction or obstetrical accidents.

Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with HMD in our study.

Mode and Method of delivery

In our study (Table 16, 17) 28% of all neonates with respiratory distress were delivered at home, while 43.5% of all cases with pneumonia were delivered outside by Dais or P/V in hospitals by untrained staff having meager facilities. We also found that 3 out of 4 neonates (75%) having MAS were delivered by emergency LSCS, the indication was prolonged labour in all three of them. Both the neonates with TTNB in our study were delivered in the hospital by emergency LSCS. 18 cases of HMD were delivered in hospital, because most of them had to be delivered by emergency LSCS. There were 5 twins in our study, which was in itself a high risk delivery.

S. Thomas et al (1981), found that there was no significant co-relation between the mode of delivery and the development of pneumonia. He also found that most of the babies with MAS were born by emergency LSCS, for which the indication was fetal distress or MSAF. In his study of 22 babies having TTNB 14 were delivered vaginally and 4 by 8 by emergency LSCS. In the same study, 10

neonates with HMD were born equally by emergency LSCS and spontaneous vaginally. However, NB Mathur commented in his study, that 51% of the neonates with respiratory distress were delivered at home, which shows that the mode of delivery had been underplayed by most previous authors.

SP Khatua et al (1979), found that out of 104 cases of aspiration syndrome, 64 were delivered abnormally due to fetal distress, prolonged labour, failed medical induction. In the same study, he found 6 cases of TTNB, out of which 4 were born by normal delivery and 2 by emergency LSCS.

Studies by SP Khatua (1979), PK Mishra (1987) and P Kumar (1999) comprised neonates which were exclusively inborn delivered by trained personnel, so the real incidence of pneumonia in out patient deliveries could not be ascertained.

Post natal history

In our present study (Table 18) we found that a history of difficulty in feeding in the post natal period with fever had a high specificity for diagnosing pneumonia. Fever post maturity also had a high specificity, but (0%) sensitivity, in the case of post maturity. 47.8% of cases had an onset of respiratory distress within 15 hours of birth and were later diagnosed as pneumonia.

In the study by SP Khatua, out of 104 cases of aspiration syndrome 41 had history of meconium staining of amniotic fluid (MSAF) with or without staining of cord, skin or nails. Out of 104 cases, 14 neonates were preterm, 87 were term and 3 were post term.

In our study (Table 19) meconium staining of cord, liquor and nails had a 100% sensitivity, specificity and predictive value for MAS. Post maturity (n=2 out of 4) also had a 100% specificity and positive predictive value in cases diagnosed as MAS.

In our study 75% of neonates with meconium aspiration syndrome developed respiratory distress within 8 hours of birth.

In the study by Thomas et al, out of 14 cases with MAS, 4 were preterm and rest were term. Most of the babies were born by emergency LSCS and indication was MSAF (8 out of 14).

In our study (Table 20), all the 21 neonates with HMD had a gestational age < 34 weeks. Both weight and gestational age had the highest sensitivity (89.6%) (93.1%) and negative predictive value (89.6%) (100%) respectively for diagnosing HMD. 71.4% neonates with HMD developed respiratory distress within 6 hours of birth. In a study by SP Khatua, out of 16 neonates with HMD, 15 were premature, while in a study by Thomas et al, all the ten infants with HMD were preterms.

Apart from a difficulty in feeding (50%), none of the other post natal factor could be associated with TTNB. 100% cases later diagnosed as TTNB presented with respiratory distress within 4 hours of birth (Table 21).

Investigations

It was our endeavor to identify cases of pneumonia responsible for respiratory distress in neonates, for which we had to resort to certain investigations enumerated in various texts by different authors. CRP was one such test whose high specificity has been proved in studies by NB Mathur et al (2002), and Mathai et al (2004) in diagnosing infections in neonates. In the study conducted by us (Table 23), we found the values for sensitivity (60%), specificity (92.6%), PPV (87.5%) and NPV (73.5%) for CRP. In comparison to other indicators of infection CRP is the single best indicator after blood culture in diagnosing early onset sepsis (EOS) (Table 24). According to Mathai et al, sensitivity, specificity and positive and negative predictive values of CRP estimation at 24 hours of age for diagnosis of early onset of sepsis using > 6 mg/L as cut off were 80%, 60%, 7.7% and 98.6% respectively. NB Mathur et al, got sensitivity and specificity of CRP as 54.3 and 90% respectively. CRP earns its respect in being a quick indicator which increases its utility. Although, its sensitivity in our study

was low (60%), if utilized with caution this test can help in reducing indiscriminate antimicrobial use in the newborn.

Studies by S Thomas et al (1979), Mishra et al (1991) and NB Mathur et al (2002) have mentioned utility of micro-ESR band cells and blood culture sensitivity in identifying EOS. But apart from NB Mathur, none of them have discussed their specificity and predictive values in detail. In our study (Table 23), specificity for Micro-ESR was 100% and sensitivity was 26%. In the study by Mathur et al, micro-ESR had a specificity of > 90% but a very low sensitivity 32%. We had a different experience with band cells and toxic granules, our specificity was close to the studies by NB Mathur i.e. > 90% but sensitivity was very low 13%, in contrast with 52.4% in the study by NB Mathur et al.

Several authors have stressed the utility of blood culture positivity in identifying cases of pneumonia, to mention a few Bhakoo (1979), Mishra et al (1991), Shakuntala et al (1978), NB Mathur et al (2002).

In the present study (Table 21), the percentage of definitive pneumonia (based on isolation of bacteria) and probable pneumonia (blood culture negative) were 39.1 and 34.8% respectively. This was close to that found in the study by Mathur et al, where definitive pneumonia was 37.9% and probable pneumonia 47.6%. This was

identical to that observed by Webber et al (1990). In our study (Table 28), the bacterial isolation percentage 56.5%, which is slightly higher than that reported by earlier authors. This could be due to the promptness in sending the blood culture samples before administration of antibiotics.

Whereas Bhakoo et al (1980), concentrated on the variety of Gram positive and negative bacteria isolated, Mishra et al (1991), went one step ahead in co-relating probable sepsis and definitive sepsis on the basis of blood culture positivity.

In a study by Mishra et al (1991), a bacterial etiology of pneumonia was found in 36.4% cases, Shakuntala et al (1978), found it to be 44%. In the study by NB Mathur et al (2002) the percentage of bacterial etiology of pneumonia was established in 47.5% neonates.

8.7% cases in our study (Table 21), had only sepsis screen positive. In the cases studied by Mathur (2002), 4.8% neonates had only sepsis screen positive. No earlier study has stated detailed diagnostic criteria for pneumonia in neonates utilizing blood culture or sepsis screen positivity.

Amongst 17 x-ray chest positive cases in pneumonia in our study, 11 cases showed alevolar infiltrates (47.8%), 4 cases showed diffuse haziness (17.3%), 2 cases showed lobar consolidation (8.6%), while 6 cases had chest x-ray clear (26.1%).

Chest x-ray and clinical signs (Table 21) alone would have missed the diagnosis of pneumonia in 26% cases and these had to corroborated with sepsis screen and blood culture. Mathur et al, found this data to be 15%, no other study was available for comparison.

In the present study, X-ray chest was positive in 50% cases of TTNB. Chest x-ray showed changes pertaining to MAS in 50% cases. In HMD, only 33.3% cases turned out to be chest x-ray positive. Rest other investigations were negative in all these three diseases i.e. HMD, TTNB, MAS and diagnosis was aided by clinical history and examination. No study was available for the comparison of chest x-ray positivity in the above disorders.

Bacterial isolation

The bacterial isolates in our study (Table 28) are consistent with the earlier studies which suggest an increasing trend of Klebsiella (61.5%, in our study). In the present study Staph aureus was found only in 2 cases (15.4%), while E.coli was responsible for pneumonia in 3 cases (23.1%). Other studies in the past which had hinted an increasing incidence of Klebsiella are S. Thomas et al (1979), ON Bhakoo (1980) (20.5%), JN Mishra et al (1985), S Mishra et al (1991) (11.3%), M Singh (1991), Mathur et al (2002) (57.9%). No cases of streptococcus pneumoniae were found as compared to Mishra et al

(1991), who found it in 10 cases (22.4%) and Shakuntala (1978) (20%). Bhakoo et al (1979) and Jeffery et al (1979) had shown higher incidence of Gram negative septicemia in neonates having early onset sepsis. This is again proved by our study, which shows a higher incidence of Klebsiella, which is a Gram negative bacteria.

No study so far had evaluated usefulness of ciprofloxacin in combating serious infections. It was our endeavor to find the antibiotic sensitivity of the bacterial isolate from our cases of pneumonia. The best coverage in our study (Table 29), has been shown by ciprofloxacin (84.62% cases) followed by ofloxacin and chloramphenicol 76.92% and 61.5% respectively. Amikacin was effective in only 23.08% cases.

Study by JN Mishra et al (1985), found all Gram negative bacteria sensitive to Amikacin, and staph aureus sensitive to methicillin / cloxacillin. We share the experience of Amikacin sensitivity to Gram negative bacteria (E.coli) in our cases too. S Mishra et al (1991), stated that gentamycin + chloramphenicol gave the best coverage 87%, followed by cloxacillin + gentamycin (76%). Similarly, cloxacillin and erythromycin showed 95% and 60% efficacy against staphylococcus pyogenes.

Fatality

In our study, respiratory distress was responsible for 28.7% of all the fatalities in the NICU. This was similar to the data found in the study by NB Mathur et al, where it was 32% of all mortality. The mortality figures were 52% for HMD in our study and 75% for MAS. The mortality figures were 81.2% for HMD in studies by SP Khatua and 100% by NB Mathur. The mortality rate for MAS is 30% by SP Khatua and 50% by Mathur et al. Mortality figures for various disorders found by S Thomas et al were pneumonia (22.4%), MAS (14.3%) and HMD (100%).

In the study by SP Khatua, the incidence of morbidity and mortality of respiratory distress amongst various birth weights was

Weight	No. of cases	%	No. expired (%)
1.6 – 2 Kg	44	24%	32 (72%)
2.1 – 2.5 Kg	55	30.3%	13 (23.7%)

We also have similar data in our study, these are 39% low birth weights (< 2.5 Kg) in pneumonia with 57.1% mortality rate. Since, there were 2 neonates with birth weight less than 2 Kg having pneumonia and both of them expired the mortality rate was 100%. In our study, 100% of low birth weight neonates with HMD expired because of their disease.

Summary

&

Conclusion

Summary and Conclusions

The present study was conducted on 50 neonates, admitted in NICU of the Department of Pediatrics, M.L.B. Medical College, Jhansi from November 2003 to October 2004, with respiratory distress. The present study was undertaken with the following aims:

1. To find the causes of respiratory distress in neonates brought to our Neonatal Intensive Care unit with symptoms suggestive of respiratory disorder.
2. To evaluate clinical signs like cough, difficulty in feeding, cyanosis, respiratory rate, chest retractions, flaring of alae nasi and adventitious sounds for diagnosis of neonatal pneumonia.
3. Determine bacterial etiology of neonatal pneumonia.
4. To study the sensitivity pattern of the prevalent bacteria in neonatal intensive care unit.

The present study comprised of neonates presenting with respiratory distress delivered in the Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi and elsewhere, but admitted in our Neonatal Intensive Care Unit (NICU). The study was conducted on the spectrum of respiratory distress, signs and symptoms, clinical history and investigations suggestive of four disorders, i.e. Pneumonia, Transient tachypnoea of the newborn,

Hyaline membrane disease (HMD) and Meconium aspiration syndrome (MAS).

The blood samples were taken from the peripheral vein for investigations, and were subjected to sepsis screen (TLC, DLC, Micro-ESR, CRP, Band cells and toxic granules), blood culture. The samples were send to the emergency pathology and Department of Microbiology, M.L.B. Medical College, Jhansi for investigations. The neonates were send for radiological investigations also.

- In our study, pneumonia was the leading cause of respiratory distress with an incidence of 46%, followed by Hyaline Membrane Disease (HMD) 42%, Meconium Aspiration Syndrome (MAS) 8%, and Transient Tachypnoea of Newborn (TTNB) 4% respectively. Respiratory distress formed 30% of all the admissions to our NICU.
- The male : female ratio of neonates developing respiratory distress was 2.3:1.
- The mean birth weight for neonates developing pneumonia was 2.2 Kg, 1.4 Kg for Hyaline Membrane Disease (HMD), 3.02 Kg for Meconium Aspiration Syndrome (MAS) and 2.6 Kgs for Transient Tachypnoea of Newborn (TTNB)
- 14 (60%) of our cases developing pneumonia were fullterm, while nine (40%) were preterms in this study.

- In our study all the 21 neonates with Hyaline Membrane Disease (HMD) had a gestational age < 34 weeks. All the 21 neonates were low birth weight. 18 of them were less than 2000 gms and remaining 3 of them were of 2 Kg. Both weight and gestational age had the highest sensitivity (89.6%) (93.1%) and negative predictive value (89.6%) (100%) respectively for diagnosing HMD.
- Cough, adventitious sounds & cyanosis had high specificity in diagnosing neonatal pneumonia, while difficulty in feeding, RR > 60/minute, flaring of alae nasi and chest retractions had high sensitivity for diagnosing pneumonia.
- The mortality in non-tachypnoeic as compared to tachypnoeic cases was significant. In our study, of 23 cases of pneumonia, we found only two cases with RR < 60 (8.7%), but the mortality was 100% and both of them had gestational age < 34 weeks and weight < 2 Kg.
- In our study, 11 mothers had a history of Prolonged Rupture Of Membranes (PRM) (10), maternal fever (2), leaking per vaginum (6). These factors had high specificity and positive predictive value in neonates developing pneumonia.
- None of the factors like maternal fever, prolonged rupture membranes, leaking per vaginum or foul smelling liquor was found

to have any association at all with transient tachypnoea of newborn (TTNB).

- Except for a history of fetal distress, none of the factors like Prolonged Rupture of Membranes (PRM), maternal fever, leaking per vaginum (LPV) had any association at all with meconium aspiration syndrome (MAS). Fetal distress had a high specificity and negative predictive value for MAS.
- Mothers of neonates with Hyaline Membrane Disease (HMD) had association with Prolonged Rupture Of Membranes (PRM) and L P/V. In our study, 5 mothers of neonates with HMD had PRM and 5 had leaking per vaginum (L P/V). Probable explanation could be that these factors were indirectly also responsible for preterm labour and birth.
- Prolonged labour has a high specificity (88.8%) for neonates having pneumonia.
- Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with Transient Tachypnoea of Newborn (TTNB).
- Prolonged labour and a history of poor cry or resuscitation in newborn have a high specificity for Meconium Aspiration Syndrome (MAS). History of poor cry in natal history had a 100% positive

predictive value (PPV) for neonates developing respiratory distress due to MAS.

- Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with Hyaline Membrane Disease (HMD) in our study.
- 28% of all neonates with respiratory distress were delivered at home, while 43.5% of all cases with pneumonia were delivered outside by Dais or P/V in hospitals by untrained staff having meager facilities.
- We also found that 3 out of 4 neonates (75%) having MAS were delivered by emergency LSCS, the indication was prolonged labour in all three of them. Both the neonates with TTNB in our study were delivered in the hospital by emergency LSCS. 18 cases of HMD were delivered in hospital, because most of them had to be delivered by emergency LSCS.
- History of difficulty in feeding in the post natal period with fever had a high specificity for diagnosing pneumonia. Fever, absence of post maturity also had a high specificity, but 0% sensitivity, in the case of post maturity.
- In our study meconium staining of cord, liquor and nails had a 100% sensitivity, specificity and predictive value for MAS. Post

maturity (n=2 out of 4) also had a 100% specificity and positive predictive value in cases diagnosed as MAS.

- Apart from a difficulty in feeding (50%), none of the other post natal factor could be associated with TTNB.
- 100% cases later diagnosed as TTNB presented with respiratory distress within 4 hours of birth.
- We found the values for sensitivity (60%), specificity (92.6%), PPV (87.5%) and NPV (73.5%) for CRP. In comparison to other indicators of infection, CRP is the single best indicator after blood culture in diagnosing early onset sepsis (EOS).
- Specificity for Micro-ESR was 100% and sensitivity 26%.
- With band cells and toxic granules, our specificity was > 90% but sensitivity was very low 13%.
- In the present study, the percentage of definitive pneumonia (based on isolation of bacteria) and probable pneumonia (blood culture negative) were 39.1 and 34.8% respectively.
- In 8.7% cases of pneumonia only sepsis screen was positive.
- Amongst 17 x-ray chest positive cases in pneumonia, 11 cases showed alevolar infiltrates (47.8%), 4 cases showed diffuse haziness (17.3%), 2 cases showed lobar consolidation (8.6%), while 6 cases had chest x-ray clear (26.1%).

- Chest x-ray and clinical signs alone would have missed the diagnosis of pneumonia in 26% cases and these had to be corroborated with sepsis screen and blood culture.
- X-ray chest was positive in 50% cases of TTNB. Chest x-ray showed changes pertaining to Meconium aspiration syndrome (MAS) in 50% cases. In HMD, only 33.3% cases turned out to be chest x-ray positive. Rest of the blood investigations were negative in all these three disorders i.e. Hyaline Membrane Disease (HMD), Transient Tachypnoea of newborn (TTNB) and Meconium aspiration syndrome (MAS).
- The bacterial isolates in our study suggest an increasing trend of Klebsiella (61.5%).
- In the present study Staphylococcus aureus was found only in 2 cases (15.4%), while E.coli was responsible for pneumonia in 3 cases (23.1%),
- Respiratory distress was responsible for 28.7% of all deaths The mortality figures were 52% for HMD in our study and 75% for Meconium Aspiration Syndrome (MAS).
- There were 39% low birth weights (< 2.5 Kg) in pneumonia. They comprised 57.1% mortality amongst total fatality due to pneumonia. Since, there were 2 neonates with birth weight less than 2 Kg having pneumonia and both of them expired the mortality rate was

100%. 11 (52.4%) neonates out of 21 with HMD expired in our study, all of them were of low birth weight.

- The best coverage in our study, has been shown by ciprofloxacin (84.62% cases) followed by ofloxacin and chloramphenicol 76.92% and 61.5% respectively. Amikacin was effective in only 23.08% cases.
- Further long-term studies have to be done before our studies on the efficacy and long-term complications of Ciprofloxacin in treating neonates with pneumonia could be finally established.

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Working

Proforma

Working Proforma

Spectrum of Respiratory Distress disorders in Neonates

Name of the newborn :

Sex : M / F

Birth weight :

M.R.D. No. :

Mother's Education :

Socioeconomic status :

Mode of delivery – Emg. LSCS / Normal Vaginal delivery.

Any anaesthesia used (Mention if G/A).

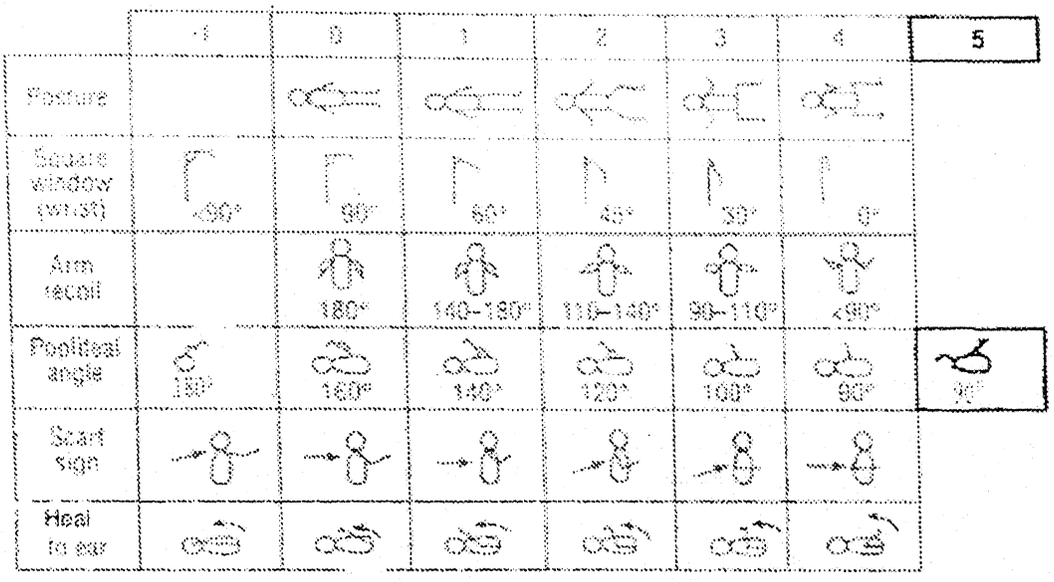
G.....P..... L.....A.....

History of previous fetal wastage

History and clinical examination		Yes	No
1.	Cyanosis	☐	☐
2.	Respiratory rate > 60 / min	☐	☐
3.	Chest retractions	☐	☐
4.	Flaring of alae nasi	☐	☐
5.	Adventitious sounds on chest auscultation	☐	☐
6.	Lethargy	☐	☐
7.	Absent neonatal reflexes	☐	☐
8.	Shock	☐	☐

New Ballard scoring for gestational age estimation of neonates

Neuromuscular maturity



Maturity Rating

Score	Weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Physical maturity.

	-1	0	1	2	3	4	5
Skin	Sticky, Friable transparent	Gelatinous red, translucent	Smooth, pink visible veins	Superficial peeling &/or rash, few veins	Cracking, pale areas, rare veins	Parchament deep cracking, no vessels	Leathery, cracked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar surface	Heel-toe, 40-50mm–1<40mm–2	< 50 mm No crease	Faint Red Mark	Anterior transverse crease only	Creases on anterior 2/3	Creases over entire sole	
Breast	Imperceptible	Barely perceptible	Flat areola no bud	Stripped areola,1–2 mm bud	Raised areola, 3-4 mm bud	Full areola, 5-10 mm bud	
Eye/ear	Lids fused loosely (-1) Tightly (-2)	Lids open pinna flat stays folded	Slightly curved pinna soft slow recoil	Well curved pinna, soft but ready recoil	Formed & firm instant recoil	Thick cartilage, ear stiff	
Genitals							
Male	Scrotum flat, smooth	Scrotum empty, faint rugae	Testis in upper canal	Testis descending, few rugae	Testis down, good rugae	Testis pendulous, deep rugae	
Female	Clitoris prominent	Prominent Clitoris, small labia Minora	Prominent Clitoris, enlarging Minora	Majora & minora equally prominent	Majora large, minora small	Majora cover clitoris & minora	

Physical Examination :

Eyes → Pupils
Eyes → Cornea

Oral cavity → Palate
Oral cavity → Lips

Neck

Skeletal system

Extremities → Upper
Extremities → Lower

Systemic examination:

CVS: GIT:

CNS:

Antenatal History	Respiratory Distress Syndrome	Meconium Aspiration Syndrome	Transient Tachypnea of the newborn	Pneumonia
1. Maternal fever > 38°C	☐	☐	☐	☐
2. Prolonged Rupture of membranes > 24 hrs	☐	☐	☐	☐
3. Leaking per vaginum	☐	☐	☐	☐
4. Foul smelling liquor	☐	☐	☐	☐
5. H/o diabetes in mother	☐	☐	☐	☐
6. H/o fetal distress	☐	☐	☐	☐

Natal History	Respiratory Distress Syndrome	Meconium Aspiration Syndrome	Transient Tachypnea of the newborn	Pneumonia
1. H/o prolonged labour	☐	☐	☐	☐
2. H/o precipitate labour	☐	☐	☐	☐
3. Traumatic Labour (Obstetrical accident)	☐	☐	☐	☐
4. Mode of delivery – ELCS/ NVD	☐	☐	☐	☐
5. Delivery Hospital / Outside by untrained Dai	☐	☐	☐	☐
6. H/o poor cry / resuscitation	☐	☐	☐	☐

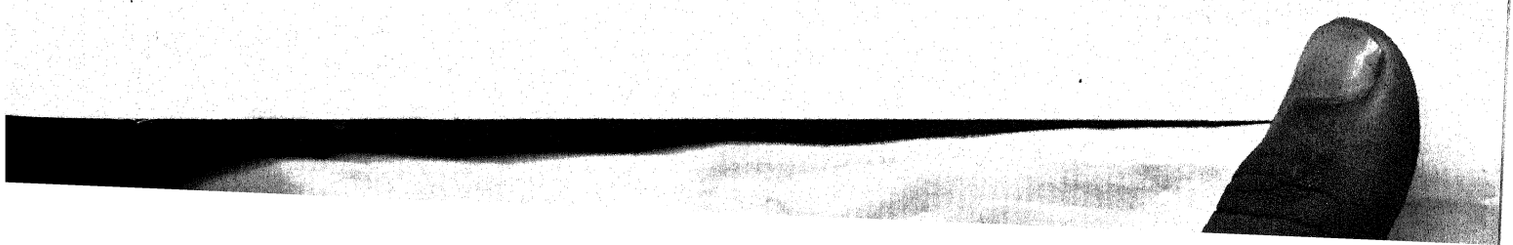
Post Natal History	Respiratory Distress Syndrome	Meconium Aspiration Syndrome	Transient Tachypnea of the newborn	Pneumonia
1. Meconium staining of Liquor /cord /Nails /Skin	☐	☐	☐	☐
2. Cough	☐	☐	☐	☐
3. Difficulty in feeding	☐	☐	☐	☐
4. Fever	☐	☐	☐	☐
5. Weight < 2000 gms.	☐	☐	☐	☐
6. Gestation < 34 weeks / Post mature	☐	☐	☐	☐
7. Duration of onset of Resp. Distress. (hours)				

Probable Diagnosis (On grounds history alone)

SEPSIS SCREEN

1. Hb% TLC DLC P_ L_ E_ M_
2. % Band cells Toxic granules Present / Absent
3. Micro–ESR mm of fall in column after 1 hour. Positive if > 13 mm fall after 1 hr
4. C-Reactive Protein Positive if values > 0.6 mg/dl

Blood culture



Culture sensitivity (if culture positive)

Chest X-ray

PROBABLE DIAGNOSIS (On grounds of history alone) :

DEFINITIVE DIAGNOSIS (After reviewing investigations) :

OUTCOME OF TREATMENT :

Discharged / Expired

1. Please collect sample for blood culture within 12 hours of starting antibiotics.
2. You are requested to send hemogram and collect one blood sample in plain vial for the purpose of CRP.